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The American Heart Journal

VOL. V FEBRUARY, 1930 No. 3

Original Communications

THE ELECTROCARDIOGRAM IN CORONARY DISEASE*

M. H. NATHANSON, M.D.
MINNEAPOLIS, MINN.

SCLEROSIS of the coronary arteries is a frequent pathological finding especially after the age of fifty. Benson and Hunter[1] call attention to the high incidence of this condition. They found 200 cases of advanced coronary obstruction in 1750 autopsies. A large number of these autopsies were coroner's cases, and this would tend to exaggerate the incidence to a certain extent. Of 339 consecutive autopsies above the age of forty from the Department of Pathology of the University of Minnesota there were twenty-seven cases of coronary disease or an incidence of approximately 8 per cent.

In a previous report[2] an attempt was made to construct a clinical picture of coronary artery disease from an analysis of the clinical data of a series of fatal cases which came to necropsy. It was found that there were variations in the clinical picture presented and four main types were described. (Table I.) Type 1 includes those cases in

TABLE I

CLINICAL TYPES OF CORONARY SCLEROSIS

CLINICAL FEATURES	NO. OF CASES
1. Heart not enlarged, congestive failure absent; symptoms of cardiac insufficiency absent; heart normal in size; blood pressure normal	43 or 37.2 per cent
2. Heart not enlarged, congestive failure present; symptoms of cardiac insufficiency present; heart normal in size; blood pressure normal	3 or 2.6 per cent
3. Cardiac enlargement, congestive failure absent; symptoms of cardiac insufficiency absent; heart enlarged; blood pressure increased	25 or 22.6 per cent
4. Cardiac enlargement, congestive failure present; symptoms of cardiac insufficiency present; heart enlarged; blood pressure usually increased	43 or 39.0 per cent

*From the Department of Medicine, University of Minnesota, Medical Service, General Hospital.

which the heart is normal in size, blood pressure is normal and symptoms and signs of congestive heart failure are absent. Type 2 has the same features as Type 1 except that congestive heart failure is present. Type 3 consists of those cases in which there is cardiac enlargement, usually some increase in arterial pressure with absence of congestive heart failure. Type 4 has the same features as Type 3 with the addition of the signs and symptoms of congestive heart failure. From the analysis of the data in this series it was apparent that clinical features especially characteristic of coronary disease are often absent and that extensive coronary disease may be present and yet escape detection by our usual clinical methods. For instance, in Type 1 there are no signs which indicate the presence of disease in the heart. There is no cardiac enlargement, the blood pressure is normal, there are no auscultatory signs diagnostic of cardiac involvement. Furthermore, the patient presents no evidence of congestive heart failure during life, since at autopsy the liver shows no passive congestion. In this group particularly it is possible for the cardiac damage to be entirely overlooked. We must rely entirely for diagnosis upon the anginal syndrome presented by the patient. If the typical anginal syndrome as described by Heberden in 1768 were always present, few errors in diagnosis would be made in spite of the absence of characteristic signs in the heart. However, the typical picture as usually described is more often absent. For example, in the analysis of our clinical data, radiation to the left arm was found in only 10 per cent of the cases. The pain was almost as frequently localized to the upper abdomen as to the chest. Furthermore, belching, nausea and vomiting were often associated so that a gastro-intestinal condition was closely simulated. Also in about 10 per cent pain was absent, and the attack consisted of an acute respiratory distress resembling bronchial asthma. These atypical subjective features and the paucity of characteristic physical signs make the diagnosis of coronary disease by our simpler clinical methods frequently very difficult.

Experimental and clinical investigations have shown that usually the electrocardiogram is definitely altered by disturbance of the coronary circulation. Studies by Smith[3] on the effect of ligation of the coronary arteries have demonstrated the sequence of changes in the electrocardiogram very clearly. Disturbance in the coronary circulation to the left ventricle in dogs is followed shortly by inversion of the T-wave. Hamburger[4] and his co-workers found similar alterations in the electrocardiogram following experimental coronary embolism by injection of a suspension of lycopodium spores into the coronary circulation. In the literature, electrocardiographic changes associated with clinical cases of coronary disease are frequently mentioned, but detailed reports on series of cases are comparatively few. Pardee[5] in an analysis of fifty cases of coronary sclerosis found the changes that appear in

Table II. Oppenheimer and Rothschild[6] show that coronary disease is the most frequent pathological condition which produces widening and notching of the QRS and alterations of the T-wave. In forty-seven cases with abnormal ventricular complexes, thirty-eight showed coronary disease at autopsy.

TABLE II

HEART DISEASE AND ABNORMAL ELECTROCARDIOGRAMS (PARDEE)

	CORONARY OCCLUSION ACUTE AND CHRONIC
Coronary T-wave	18
Downward T-wave in Lead I or Lead II or both	5
Small excursion of T-wave (low voltage)	0
Notched QRS group	2
Small excursion of QRS (low voltage)	3
Bundle-branch block	6
Normal QRS and T-wave except for R. V. P. or L. V. P.	16
Total	50

TABLE III

ELECTROCARDIOGRAPHIC FINDINGS IN 60 CASES OF CORONARY SCLEROSIS

	NUMBER	PER CENT
Inversion of T-wave	53	88
Lead I	24	40
Leads I and II	9	15
Leads II and III	17	28
Leads I, II and III	3	5
Coronary T-wave (Pardee)	13	21
Changes in QRS		
Bundle-branch block	6	10
Arborization block	2	3.3
Moderate notching	11	18
Slight notching	18	30
Low Voltage	9	15
Prolonged P-R	4	6.6
Arrhythmias		
Extrasystoles	11	18
Auricular fibrillation	4	6.6
Complete heart-block	1	1.6
Ventricular Preponderance		
Definite left	18	30
Slight left	18	30
Slight right	2	3.3

The present report consists of an electrocardiographic study of sixty cases of coronary disease. The diagnosis of coronary disease was made either from autopsy findings or from a characteristic clinical picture and outcome. Only those cases were selected in which the electrocardiogram showed a deviation from the generally accepted normal. This analysis therefore does not attempt to determine the incidence of an abnormal electrocardiogram in coronary disease. There is no

doubt that coronary disease may exist without any definite electrocardiographic abnormality. Pardee's analysis indicates significant changes in about 70 per cent of cases. The present report is concerned with a statistical analysis of the electrocardiographic alterations in those cases of coronary sclerosis in which the electrocardiogram showed some distinct abnormality. Table III is a summary of these findings.

The most frequent electrocardiographic deviation was inversion of the T-wave which was present in 88 per cent of the cases. The possible effect of digitalis was excluded in all cases. This observation agrees with that of Pardee who found T-wave inversion in twenty-three of thirty-four cases in which there was an abnormal electrocardiogram. Willius and Brown[7] noted T-wave inversion in 14 of 17 abnormal electrocardiograms of coronary sclerosis. Smith[3] found that ligation of the ramus descendens or circumflex branch of the left coronary artery in dogs is uniformly followed by inversion of the T-wave. Ligation of the right coronary vessels produces no such change. Apparently this cannot be wholly applied to the human heart. In two of the autopsied cases in this group there was a thrombus occluding the right branch. In one instance, there was inversion of the T-wave in Lead I and in the other in Leads II and III. This may be explained by individual variations of the coronary distribution in the human heart. Pardee[5] has described a peculiar type of T-wave which he considers as specific for coronary disease and which he has designated as the coronary T-wave. The characteristic features are a downward sharply peaked T-wave with an upward convexity of the S-T or R-T interval. In Table II it will be noted that of twenty-three instances of T-wave inversion eighteen showed a coronary type of T-wave. In the present series there were fifty-five cases of definite T-wave inversion with but thirteen showing this type of wave. These observations indicate that although the coronary T-wave of Pardee is frequently associated with coronary disease, ordinary T-wave inversion without any special features is equally significant for the diagnosis of coronary sclerosis. It is not to be concluded that inversion of the T-wave is specific for coronary arterial disease. Experimentally it is possible to produce negativity of the T-wave by other means than by vascular occlusion, such as by cooling the apex of the heart,[3] by introducing certain substances such as digitalis[8] or diphtheria toxin[9] and by stimulation of the vagus nerve.[10] Likewise, clinically, inversion of the T-wave is seen in cases of hypertension in the absence of coronary disease, especially with left ventricular preponderance, and also less frequently in valvular disease. T-wave negativity is also found following severe diphtheria[9] and in myxedema.[12] There is little doubt, however, that it is found with the greatest frequency in coronary disease. The less frequent causes of T-wave inversion can usually be easily

excluded and particularly in the absence of cardiac enlargement and congestive heart failure as occurs in Type 1, T-wave inversion may be considered as practically pathognomonic of coronary sclerosis.

Alterations of the initial portion of the ventricular complex, the QRS, were less frequent than changes in the T-wave. There were six cases showing the features of bundle-branch block; a ventricular complex of diphasic character, high amplitude with widened notched QRS. Five of the electrocardiograms of bundle-branch block were those which are generally accepted as indicating right bundle block. There was one instance of left bundle block. There were two cases of widened, notched QRS of low amplitude, the features as described by Oppenheimer and Rothschild of arborization block. It is generally accepted that aberration of the QRS is an evidence of disturbance in the intraventricular conduction. Although rare cases of transient or intermittent bundle block have been reported,[12] most abnormalities of the QRS of this type are permanent and fixed. This suggests that the pathological condition affecting the architecture of the intraventricular conduction system is a permanent anatomical type such as myocardial fibrosis. Clawson[13] has shown that extensive fibrosis in the ventricles is almost entirely due to coronary disease and also that there is a close relation between the location and extent of the fibrosis and the distribution and degree of coronary sclerosis. It is not surprising therefore to find those abnormalities of the QRS associated with coronary disease.

Of considerable interest is the frequency of lesser degrees of notching of the QRS without increase in the time interval. The correlation of such deviations with pathological change in the heart is less definite, since such changes are found associated with normal hearts, especially in the third lead. However, certain observations indicate that these minor changes in the QRS are much more frequent in cardiac disease. Wedd[14] studied thirty cases showing slight notching of the QRS, and definite cardiac lesions were present in twenty-one. Willius[15] believes that notching and slurring of the QRS in isolated derivations indicate local disorders in the myocardium affecting the conducting system. Pardee[16] states that such aberrations of the QRS can be considered normal only when found in one lead and that lead being of relatively small excursion. If present in two leads it can be considered normal only when the notching occurs near the base line. It is never normal according to Pardee to find notching in three leads or near the peak of the R in a lead of relatively large excursion. Ferguson and O'Connell[17] in an electrocardiographic study of 1812 healthy midshipmen at the Naval Academy found notching of the QRS in about 10 per cent. In every instance it was confined to Lead III. In the present series of cases of coronary disease there were twenty-nine cases showing minor notching of the QRS, an incidence of 48 per cent as

compared with 10 per cent in the above-mentioned normal group. Furthermore, of these twenty-nine cases only five showed the notching limited to Lead III. In the remaining twenty-four cases it was present in the other leads, and in eighteen instances it was present in more than one lead. From these observations it seems justifiable to conclude that minor notching of the QRS, especially if present in Leads I and II, is frequently indicative of pathological changes in the myocardium and should arouse a suspicion of coronary disease.

Electrocardiograms of low voltage were noted in nine cases, or 15 per cent of the series. The records were considered as being of low voltage when the maximum amplitude of the QRS in all leads was less than 5 mm. above or below the base line. There is a difference of opinion concerning the significance of this type of electrocardiogram. Sprague and White[18] analyzed fifty-seven cases, of which thirty-four showed evidence of arterial sclerotic heart disease, ten were diagnosed as myxedema and thirteen classified as miscellaneous. These observers conclude that low voltage is of definite significance as indicative of myocardial involvement. Willius and Killins[19] more recently found 140 records showing these features in the material at the Mayo Clinic, or an incidence of 0.3 per cent. Thirty-two per cent of these cases showed evidence of cardiac disease, the remaining 68 per cent included a variety of conditions not associated with heart disease. These observers do not believe that electrocardiograms of low voltage unassociated with other abnormalities indicate any serious myocardial disease. The observations of Willius and Killins unquestionably show that low amplitude records may be found without cardiac damage. However, as with minor notching of the QRS, the question of relative frequency in cardiac disease as compared with normal is of importance. Willius and Killins in their survey of general material at the Mayo Clinic found an incidence of 0.3 per cent as compared with 15 per cent in our group of coronary disease. The frequency of low voltage in the coronary group was therefore about fifty times that of the series reported by Willius and Killins. It would seem, therefore, that this deviation in spite of its occasional occurrence in the normal cannot be entirely disregarded as an evidence of myocardial involvement.

Prolongation of the P-R interval occurred in but four cases, or 6.6 per cent. Every case of increased P-R interval was associated with an abnormal ventricular complex of bundle-branch block. It is apparent that the junctional tissues are infrequently affected in coronary disease and then only when there is vascular obstruction to the septum so that one of the main branches of the bundle is involved. There was one instance of complete heart-block which also showed auricular fibrillation.

Arrhythmias.—The most frequent irregularity was the extrasystolic type which was present in eleven cases or 18 per cent. Auricular

fibrillation occurred in but four cases or 6.6 per cent. In every instance the auricular fibrillation was associated with signs of congestive failure. It has been a matter of common observation that angina pectoris is very infrequently associated with auricular fibrillation. In the present series there was no case of coronary disease of Type 1 or Type 3, i.e., cases with only the anginal syndrome, which showed auricular fibrillation. The case of complete heart-block with auricular fibrillation has already been mentioned. Paroxysmal tachycardia, especially of the ventricular type, has been noted with coronary disease. Although there were several histories suggesting the presence of such attacks, this arrhythmia was not present in any case at the time of taking the record.

Ventricular Preponderance.—There were thirty-eight cases which could be considered as showing some degree of ventricular preponderance. The bundle-branch group was not considered and was not included. Excluding this group any alteration in the direction and amplitude of the QRS which in any way suggested preponderance curves was included. Eighteen cases, or 30 per cent, showed the features of a definite preponderance, left ventricular in every case. There were eighteen cases showing a slight degree of left preponderance and but two of slight right preponderance. There are undoubtedly two chief reasons for the frequency of left ventricular curves. First, coronary disease is often associated with hypertension and cardiac enlargement of the left ventricular type, and this accounts for most of the definite left preponderance curves. Second, it is well known that the form of the normal electrocardiogram is to a considerable degree dependent on the position of the heart. This has been emphasized by Herrmann and Wilson[20] in their study of ventricular preponderance. The characteristic electrocardiogram of the stout, broad-chested individual with a transversely placed heart shows either a low QRS in Lead III or one which is directed downward to some degree. This undoubtedly explains the majority of slight left preponderance curves since it is in the hypersthenic type that coronary disease most commonly occurs. The frequency of left preponderance curves in contrast to those of right preponderance may have some practical application. On several occasions the following condition has been encountered. In an elderly individual with a previous history of a cough and paroxysmal dyspnea followed by signs of congestive heart failure it is often necessary to differentiate between primary right heart failure and coronary disease with congestive failure. Since most cases of primary right heart failure show a definite right preponderance, coronary disease can be excluded largely on this feature alone.

Following is a group of illustrative cases showing the various types of electrocardiographic changes in coronary disease.

CLINICAL REPORTS

CASE 1.—A. G., male, aged 57 years, suffered from attacks of precordial distress three to four years. He was in the hospital for several months for these attacks and discharged with a diagnosis of hypertension and coronary disease October 24, 1927. Two days later he had a severe attack of precordial pressure lasting several hours. After two days he had another severe attack and was again admitted into the hospital. The blood pressure was 230/130 mm.; there were many moist râles in the lungs. During his stay in the hospital he had many attacks of acute orthopnea lasting up to several hours, when he would sit up gasping for breath, his lungs were filled with high-pitched bronchial râles and many coarse bubbling râles. At times there were intervals of several weeks be-

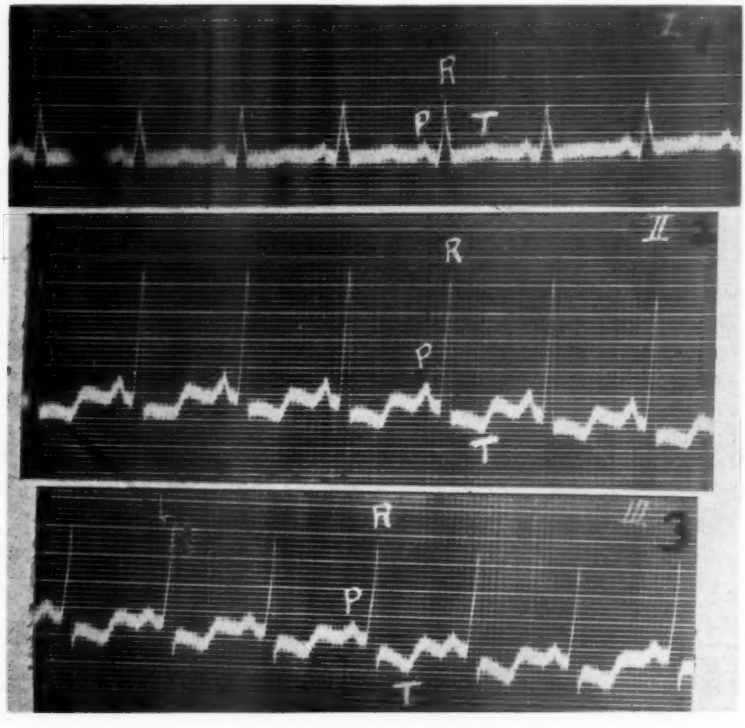


Fig. 1.—Case 1. Leads I, II and III; inversion of the T-wave in Leads II and III. Autopsy showed marked thickening of the small branches of the coronary arteries and areas of fibrosis and necrosis in the myocardium.

tween attacks, at others times they occurred daily. He was in the hospital from October 28, 1927, until he died, May 15, 1928. He had fever for ten days preceding his death and signs suggesting consolidation during the last few days. He apparently died of bronchopneumonia.

At autopsy the pericardial cavity showed 50 c.c. of clear fluid, the heart was enormously enlarged, weighing 990 gm., and there was extreme hypertrophy of the muscle of the left ventricle. There was a large area of scarring with considerable depression in the muscle of the left ventricle. There was very marked thickening of the small branches of the coronary arteries but no actual thrombosis. Microscopically the heart showed marked myocardial fibrosis and some small areas of necrosis with hyalin change. The right lung showed bronchopneumonia. An

electrocardiogram taken October 29 (Fig. 1) showed a definite inversion of the T-wave in Leads II and III with some slurring of the QRS. Repeated electrocardiograms taken during his stay in the hospital showed similar findings.

CASE 2.—F. H., male, aged 70 years, admitted to the hospital October 27, 1926, died November 16, 1926. His complaints were pains in the chest, cough, and shortness of breath. He had had a dry cough for ten days. On the day before admission on getting out of bed he had been seized with a severe pain in the anterior chest. During the attack, which lasted about three hours, he perspired a great deal. In the evening the pain returned, and he described it as a pressure being exerted on an area about the size of the fist to the left of the middle sternum. The pain was intense but there was no radiation. He had had no previous attacks of this kind. On examination there was some dyspnea, some cyanosis of the lips, pulse rate was 60, radial arteries were very sclerotic, heart seemed slightly enlarged, heart sounds were distant, there were no murmurs, blood pressure was 125/75 mm. He had an occasional attack of pain while in the hospital but seemed to be getting along very well. He died suddenly, however,

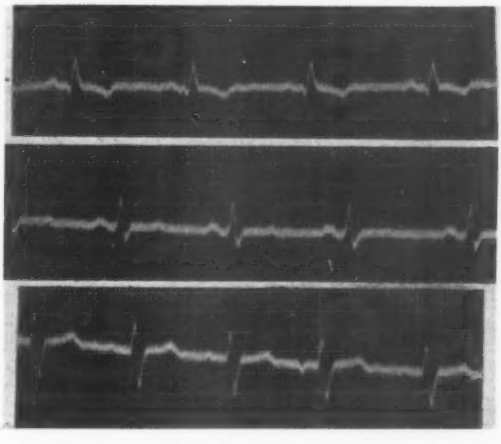


Fig. 2.—Case 2. Leads I, II and III showing inversion of the T-wave in Lead I. Autopsy showed the lumen of the left coronary artery practically obliterated by sclerosis, numerous areas of softening and fibrosis in the heart muscle.

November 17, 1926. Leucocyte count was 14,000, urine was negative. Three electrocardiograms were taken during the stay in the hospital and all showed a definite inversion of the T-wave in Lead I. The first two tracings showed ventricular extrasystoles and some notching of the R in Lead I. At autopsy there was a slight increase of fluid in the pericardial cavity, the heart weighed 540 grams, there were numerous areas of softening in the muscle and fibrosis, the left coronary artery was markedly sclerotic, but it was impossible to demonstrate thrombosis. Lumen of the artery was practically obliterated.

CASE 3.—N. R., female, aged 86 years, admitted to the hospital April 15, 1927, died April 22, 1927. She had had attacks of precordial pain and epigastric distress for five years. Her previous health had been good. April 2 she had a severe attack of pain starting in the precordium and radiating to the left shoulder and left side of the neck and left arm. She was holding an infant in her arms at the time and raising it up and down. A physician diagnosed the condition as neuritis. On the morning of admission she had another severe attack of a similar nature. She was then brought to the hospital. On admission her pulse was 84,

extrasystoles were present, the heart sounds were muffled, there were no murmurs, the heart did not appear enlarged to percussion. The blood pressure was 96/60 mm. and leucocyte count 11,300. During her stay in the hospital she had frequent attacks of epigastric and precordial pain requiring the use of morphine. On the day of her death she had a very severe attack, became cyanotic, and died in the attack. At autopsy the visceral and parietal pericardium at the apex of the left ventricle were adherent. Weight of the heart was 400 gm., and there was a widespread softening and thinning of the left ventricle. Just above the apex the softening was so marked that there was almost a rupture of the heart wall. There was a thrombus of the entire descending branch of the left coronary artery, and this artery showed marked sclerosis of its walls. The liver showed some chronic passive congestion. An electrocardiogram showed a definite inversion of the T-wave in Leads I and II with arching of the R-T interval, described as characteristic by Pardee.

CASE 4.—O. S., male, aged 64 years, admitted May 10, 1923, in serious condition, died the afternoon of the same day. Patient was seen at his home three days

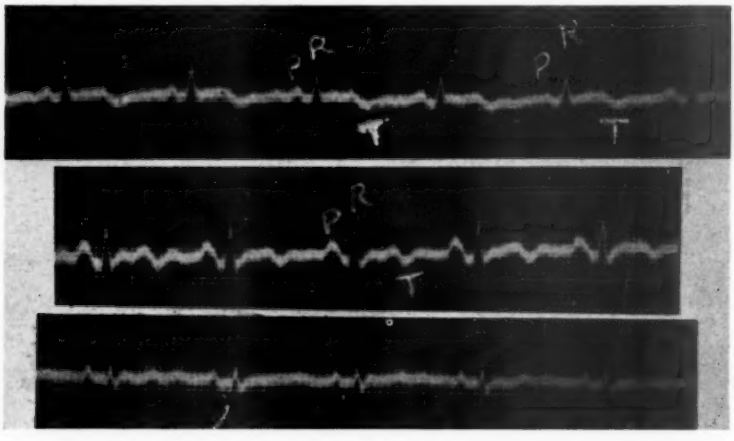


Fig. 3.—Case 3. Leads I, II and III showing inversion of the T-wave in Leads I and II with upward convexity of the R-T portion. (Coronary T-wave of Pardee.) Autopsy findings were sclerosis and thrombosis of the left coronary artery with widespread softening and thinning of the left ventricle.

before admission when he had complained of a constant pain in the left chest and left arm of several days' duration. He had treated it as rheumatism. The pain also radiated to the left side of the neck and the suboccipital region. Except for the pain, the patient appeared to be in good condition and examination of the heart was negative. The day before admission the patient began to vomit persistently, at times the vomitus being dark brown in color. He felt weak and dizzy prior to the vomiting and later became short of breath. His past history was essentially negative. Physical examination showed a well-developed and well-nourished man complaining of severe pain in the chest and vomiting. There was a diffuse slaty cyanosis, no edema, the heart did not appear enlarged. The heart sounds were muffled, pulse was fairly rapid and weak, blood pressure was not obtainable, extremities were cyanotic and cold. The diagnoses considered were ruptured bleeding ulcer, some type of drug poisoning, or coronary disease. Since bleeding ulcer was considered, a transfusion was given. He died two hours after this transfusion. Electrocardiogram showed a deep inversion of the T-wave in Leads II and III. (Fig. 4.) At autopsy there was no edema, there was a general

cyanosis of the entire body, the heart weighed 440 gm., the cavity of the left ventricle was not dilated, but there was a slight increase in the thickness of the wall. The muscle showed no decrease of consistency and on section very little evidence of fibrosis. The left coronary artery showed irregular patches of intimal thickening some of which were calcareous, some of the small muscular branches showed complete occlusion. There was a nondetachable blood clot in the right coronary artery, 3 cm. from its origin. The smaller branches showed changes similar to those in the left coronary artery. There was no apparent softening of the wall in connection with the thrombus. The liver was not congested. The stomach contained about 100 c.c. of dark brown bloody fluid, there was no evidence of ulcer, there was a submucous extravasation of blood in the region of the cardia which suggested this point as a possible source of the hemorrhage. Microscopic examination of the heart showed no evidence of interstitial fibrosis in the sections examined. The thrombus in the right coronary artery showed a laminated structure, many leucocytes, fibrin and hyalinized red blood cells. In this instance there was a marked T-wave inversion with thrombosis of the right coronary artery, but no anatomical change in the region supplied by the artery

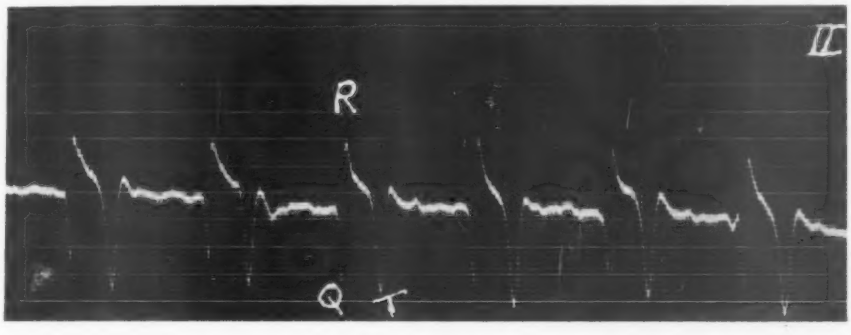


Fig. 4.—Case 4. Lead II showing deep inversion of the T-wave. Autopsy showed sclerosis of smaller branches of both coronaries and a recent thrombus in the right coronary artery 3 cm. from its origin. No softening of the myocardium.

to explain the abnormal electrocardiogram. It is evident that a demonstrable anatomical alteration in the myocardium subsequent to vascular occlusion is not necessary for the production of a high-grade electrocardiographic change.

Case 5.*—W. H. J., male, aged 69 years. Present illness began in 1921 with painful muscle cramps usually in the legs and side of the chest. Patient stated he had had these attacks during the past seven or eight years. The attacks lasted from three to fifteen minutes and were relieved by rubbing the affected muscle. The blood pressure was 152/90 mm. In October, 1925, while walking uphill he had a sudden feeling of constriction in his chest. Since that time he has had similar attacks on exertion. In November, 1925, he had a severe attack while delivering a sermon. This was relieved by nitroglycerine. Since February, 1926, he suffered from dyspnea and orthopnea at night which was relieved by nitroglycerine. Blood pressure was 128/80 mm. In July, 1926, he still complained of these nocturnal attacks, his heart showed no murmurs. In August, 1926, blood pressure was 130/80 mm. In January, 1927, he contracted an acute respiratory infection. On examination he showed some left ventricular enlargement, no murmurs, blood pressure 120/80 mm. There were some moist râles at the lung bases

*I am indebted to Dr. T. A. Peppard for the opportunity of including Cases 5 and 8.

and some edema of the lower extremities. An electrocardiogram (Fig. 5) showed the features of a right bundle-branch block. An x-ray October 15, 1925, showed MR 5, ML 10.5, total chest width 30.3 cm.

The patient was in the hospital from February to June, 1927, with signs of congestive heart failure and responded very slowly to treatment but finally improved so that he was discharged on May 25, 1927. On September 9 he again complained of attacks of asthma-like dyspnea and was very edematous. Attacks of dyspnea were relieved by ephedrin. He developed a marked oliguria and died October 16 with an anuria of two and one-half days' duration.

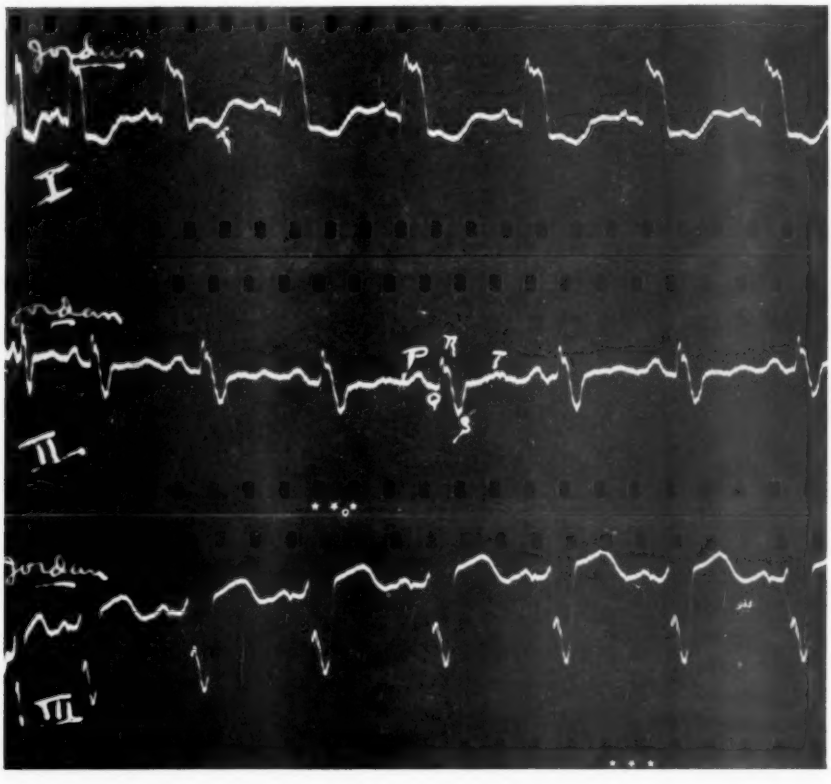


Fig. 5.—Case 5. Leads I, II and III showing right bundle-branch block. Autopsy showed extensive coronary sclerosis especially of the left coronary with almost complete closure of the anterior descending branch; lower half of the anterior part of the left ventricle markedly thinned and replaced by scar tissue.

At autopsy there was considerable edema of the extremities, the heart weighed 600 gm., there was marked hypertrophy of the left ventricle and to some degree of the right ventricle also. There was no disease of any of the valves. There was marked sclerosis of the coronary arteries, especially of the left, with almost complete closure of the anterior descending muscular branch of the left coronary. A large part of the lower half of the anterior wall of the left ventricle was markedly thin, its thickness being less than half that of the other part of the ventricle. The thin part showed a large amount of scar tissue, and on the endocardial surface there was a massive thrombus covering the entire area. The root of the aorta showed a few elevated calcified nodules on the aortic wall. The

liver showed definite passive congestion, the kidneys grossly were quite negative and on microscopic section showed only a moderate arteriosclerosis.

CASE 6.—C. H., female, aged 56 years, admitted April 25, 1927, died June 26, 1927. Patient complained of a heavy feeling in the stomach with pressure as if choking for three months, attacks of shortness of breath for the same duration. The patient had known she had diabetes for one and one-half years and had had the anginal symptoms for three months. The attacks occurred on exercise, but at times wakened her at night so that it was necessary for her to sit up to breathe. Her diabetes had been mild and insulin unnecessary. Physical examination showed a very obese woman in no particular distress. Her heart was enlarged, of the hypertension type, auricular fibrillation was present. There were no murmurs. Blood pressure was 170/100 mm., the liver was definitely enlarged, and there was a mild edema of the ankles. Electrocardiogram showed auricular fibrillation with low voltage in the first two leads with distinct notching of the QRS without widening, and depressed T-waves. The urine showed no sugar. After

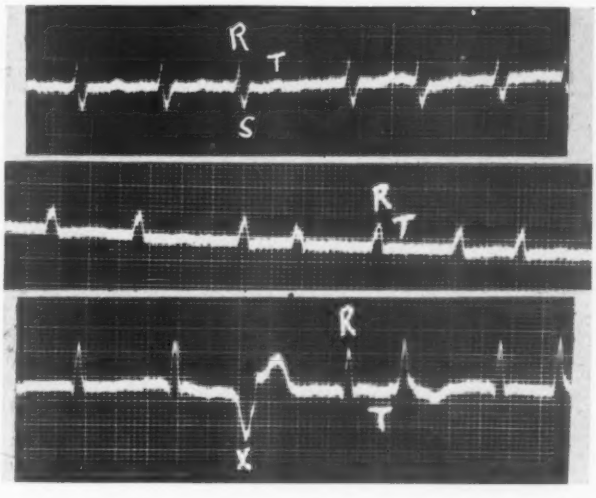


Fig. 6.—Case 6. Leads I, II and III. Auricular fibrillation and only slight alterations in the ventricular complex, slurring of the QRS in Leads I and II. Autopsy showed extreme sclerosis and thrombosis of the right coronary artery and widespread scarring of the myocardium.

a temporary improvement she gradually became weaker until her death on June 26. At autopsy the lungs showed a moderate congestion; the heart weighed 460 gm.; there was extreme sclerosis and thrombosis of the right coronary artery; the left coronary vessel showed only a moderate sclerosis; the myocardium exhibited widespread scarring, there was no definite softening. This is an example of coronary disease with widespread myocardial damage showing only minor electrocardiographic changes, a definite slurring and notching of the QRS.

CASE 7.—C. F., male, aged 66 years, admitted January 25, 1924, died February 17, 1924. Two years before the patient had a sudden pain in the chest and feeling of constriction and suffocation, pain radiating to both arms. In the past few months the patient had been wakened often at night by attacks of shortness of breath. Recently he had dizzy attacks on sudden movements such as turning his head or getting out of bed. On examination he showed some dyspnea, râles at the lung bases and many wheezy bronchial râles. There was moderate edema of

the ankles. An electrocardiogram (Fig. 7) showed low voltage in all leads, with the T-wave in the first lead leaving the R definitely above the base line. On February 17 he had an attack which was apparently a cerebral accident. His right arm and left leg became flaccid; he was unable to talk, became irrational and died four hours after the onset. At autopsy the heart weighed 420 gm. The pericardial cavity contained about 100 c.c. of slightly cloudy fluid and a few fibrin flakes. There was a mural thrombus at the apex of the left ventricle, and the myocardium at this point showed much fibrosis. The main coronary branches showed extensive sclerosis, and at one point in the left coronary the lumen was about 80 per cent occluded. The liver showed some congestion. In this instance there was extensive coronary disease, especially on the left side, showing only low voltage and changes in the R-T interval in the first lead.

CASE 8.—T. S. S., male, aged 55 years. Ten years before he had been told by a life insurance examiner that he had high blood pressure, but he had no symptoms at that time. The present illness began three years ago. After walking four or five blocks he experienced a pain in the back between the scapulae. If he continued walking, the pain would extend down both arms. If he rested, the

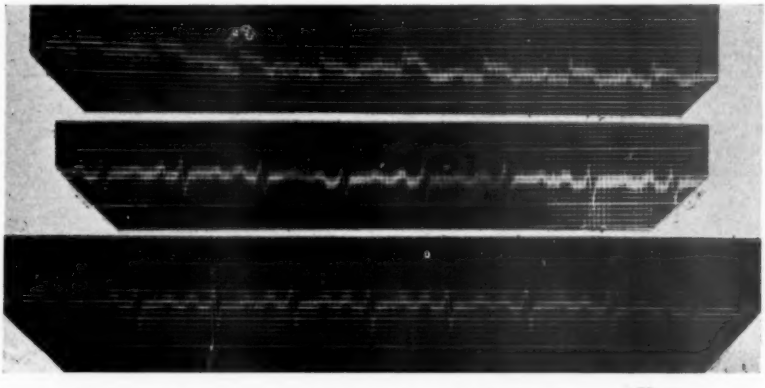


Fig. 7.—Case 7. Leads I, II and III showing only low voltage and T_1 leaving the R above the base line. Autopsy findings were extensive coronary sclerosis with the left branch almost completely occluded at some points, also marked fibrosis at the apex of the left ventricle.

pain disappeared but frequently recurred on further effort. At times he noticed that the pain would develop as soon as he began playing golf, but if he continued it would pass off. The attacks occurred on excitement as well as on exertion. The pain always localized to the middle of the back and when severe radiated to both arms. There was never any pain in chest or epigastrium. He noticed a little shortness of breath during the attacks. An electrocardiogram (Fig. 8) showed depression of the T-wave in Lead II, inversion in Lead III and slight slurring of the QRS in all leads. He developed a very severe attack while he was making an after-dinner talk twelve days before his death. Two days later a pericardial friction rub was heard. At this time he showed a temperature of 101° and a leucocytosis of 13,000, and pericardial friction was heard for two days. An x-ray film showed definite left ventricular enlargement; no murmurs were heard. Systolic blood pressure was 180 three years before, and one year before it was the same. January 7, 1926, during a severe attack systolic pressure was 138. On January 17, 1926, the patient developed a sudden attack of dyspnea while lying in bed, became unconscious and died within a few minutes.

Autopsy showed a heart weighing 550 gm. The visceral pericardium was

slightly roughened on the lower half of the right ventricle, but there was no exudate. There was a marked hypertrophy of the left ventricle with only moderate dilatation; there was no disease of any of the valves. The left coronary artery showed extreme calcification so that it had a bony hardness. The lumen was narrowed and practically occluded in several places in the descending branch to the left ventricle and in the auriculoventricular branch. Occasional small thrombotic masses were found in the narrowed lumen. There was extensive infarction of

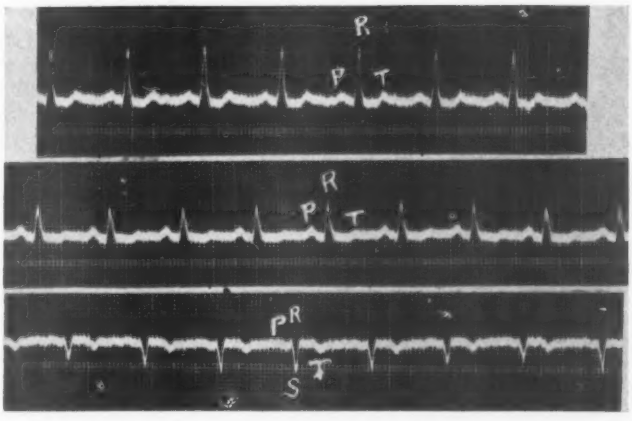


Fig. 8.—Case 8. Leads I, II and III showing only slight slurring of the QRS at the apex in all leads, depressed T-wave in Lead II and inverted T-wave in Lead III. Autopsy showed extreme sclerosis of the left coronary with marked narrowing of the lumen and extensive myocardial softening.

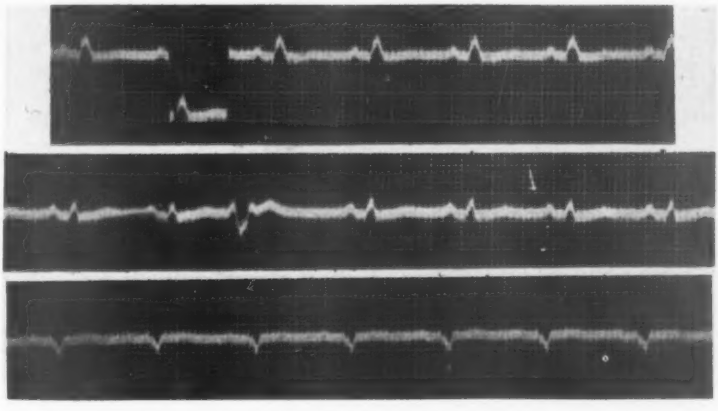


Fig. 9.—Case 9. Leads I, II and III showing very low voltage and slurring of the QRS in all leads. Autopsy showed a very severe degree of coronary sclerosis especially of the left with almost complete occlusion of the circumflex and main descending branches; myocardial fibrosis most marked at the apex.

the interventricular septum and of the lower half of the left ventricle, especially anteriorly. The myocardium in these portions was opaque and softened. There were small areas of softening in the upper half of the lower ventricle. The right coronary artery showed marked thickening of the wall and some narrowing of the lumen, but the lumen was not occluded at any point. The root of the aorta showed only occasional small yellow patches. There was a marked congestion of the liver. The pathological diagnosis was marked coronary sclerosis

with coronary thrombosis and infarction. This case illustrates extensively coronary disease with minor electrocardiographic changes.

CASE 9.—J. C., male, aged 70 years, admitted first to the General Hospital in 1928 because of pain in the extremities, swelling of the ankles, attacks of precordial pain. It was found that the patient was suffering from a definite diabetes. There was a large amount of sugar in the urine at times and blood sugar was elevated. The heart was moderately enlarged, tones distant, and blood pressure was 108/46 mm. An electrocardiogram (Fig. 9) showed low voltage with definite slurring of the QRS in all leads. He was discharged after two months in the hospital. He was readmitted in January, 1929, with dyspnea and edema. The blood sugar was 0.28 per cent, which dropped to normal on treatment and the urine became free of sugar. After eighty-one days in the hospital he was discharged very much improved. His last admission was on April 29, 1929, when he showed signs of advanced cardiac decompensation with generalized edema. The heart was enlarged to the left, there was enlargement of the liver. An electrocardiogram on this admission showed the same features as on the previous admission. On June 3 he developed an erythematous area on the face suggesting erysipelas and was transferred to the contagious ward. On the following day he suddenly became

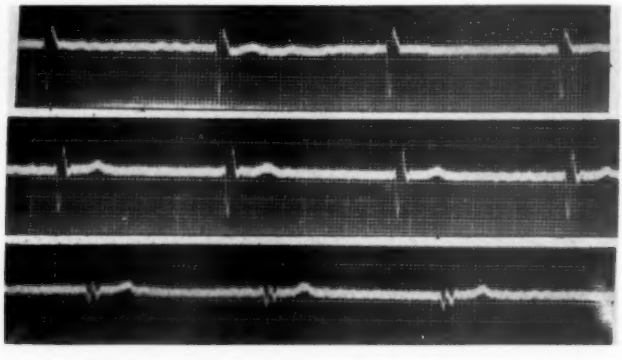


Fig. 10.—Case 10. Leads I, II and III showing auricular fibrillation and complete heart-block, also some widening of the QRS. Autopsy findings were advanced sclerosis of the left coronary artery and its branches.

cyanotic and died. At autopsy a generalized edema was present, and fluid in the abdomen. The heart weighed 400 gm., and the left ventricle was definitely dilated but showed very little hypertrophy. A very severe degree of coronary sclerosis was present, most marked on the left. The first portion of the circumflex branch to the left ventricle was almost completely closed. The main descending branch was also markedly calcified and the lumen so narrowed that in portions only a capillary opening remained, the right coronary artery was only moderately involved. The septal portion of the myocardium was quite free of fibrosis, but in the apex fibrosis was very marked and there was a definite thinning of the wall. In the wall of the right ventricle there was only one small area of fibrosis. The liver showed passive congestion, and there was a generalized arteriosclerosis present. In this case there was extensive coronary disease, especially of the left side, with definite fibrosis in the myocardium exhibiting an electrocardiogram with only minor changes, low voltage and notching of the QRS in all leads.

CASE 10.—A S., male, aged 74 years, admitted March 18, 1927, died April 27, 1927. On the day before admission he suddenly fell, striking on the left side of the head. He was not unconscious but the fall was followed by a definite left-

sided hemiplegia with difficulty in speech. Previous history was not important with the exception that he had shortness of breath on exertion for the past seven years. On examination the patient was dyspneic, with Cheyne-Stokes respiration, a left hemiplegia was present, blood pressure was 230/70 mm., radial pulse 36, there were extrasystoles present. The heart seemed definitely enlarged to the left, and there was a soft systolic murmur at the apex. The patient seemed to improve as far as the paralysis was concerned but the dyspnea and orthopnea continued, and the blood pressure remained high. On the morning of the day before his death he became unconscious, and the nurse reported that he had a convulsion preceding this. The pulse could not be felt, faint heart sounds could be made out 10-12 times a minute, which would suddenly change to 44 per minute. He was given artificial respiration and was conscious by evening but had convulsive movements of both arms and legs. On the following morning he had a similar attack. On this occasion the pulse could not be felt and no heart sounds were heard. He was given 2 c.c. of adrenalin into the heart and in a few seconds the heart began to beat at a rate of 120 up to 132. It seemed totally irregular. It remained rapid for ten minutes and then suddenly stopped. He was given another injection of adrenalin but there was no response.

Two electrocardiograms were taken (Fig. 10) during his stay in the hospital. Both showed a ventricular rate of 40 with regular rhythm. The P-wave was absent, and the diastolic period showed the typical irregular oscillations of auricular fibrillation. The electrocardiogram, therefore, showed auricular fibrillation with complete auriculoventricular dissociation. The duration of QRS was increased to from 0.14 to 0.16 of a second. There was some slurring in Leads I and II and a definite notching in Lead III. The downward QRS in the first lead gives the tracing the features which are suggestive of left bundle-branch block. At autopsy the pericardial cavity was widely dilated, the heart weighed 705 gm., and there was an advanced sclerosis of the left coronary artery and its branches. Examination of the region of the bundle of His showed no fibrosis grossly. There was very little fibrosis throughout the myocardium. Microscopic examination of the bundle of His showed some change consisting of vacuolization and thinning of the fibers. The liver showed evidence of chronic passive congestion.

CLINICAL MATERIAL

A detailed analysis of the clinical data is not included in this report. In ten cases the clinical features were those which are considered as characteristic for an acute coronary occlusion by a thrombus. This diagnosis was confirmed by autopsy in four instances. The remaining fifty cases presented the picture of chronic narrowing of the coronary vessels. Of the sixty cases, twenty-five could be classified as belonging to Type 1 following the classification of Table I. This group differs from the other types of coronary disease in that definite cardiac enlargement, hypertension, and congestive heart failure are absent. As mentioned previously, this type of coronary disease often presents considerable difficulty in diagnosis. Analysis of the electrocardiographic findings of these twenty-five cases reveals no essential differences from the remainder of the series. There were two instances of right bundle block and one of low voltage. In the remaining records the significant alteration was in the T-wave. From pathological studies the similarity of electrocardiographic findings in the various types of coronary sele-

rosis is to be expected, since the intensity of the sclerotic change bears no relationship to the presence or absence of cardiac enlargement or of congestive heart failure. Coronary sclerosis and myocardial fibrosis is present in hearts of normal size, associated with normal livers, with the same degree of severity as in enlarged hearts with livers showing passive congestion.

POST-MORTEM MATERIAL

Sixteen cases came to autopsy, all showing extensive coronary disease. No attempt will be made in this report to correlate the extent and site of the anatomical change with the form of the electrocardiogram. Of these sixteen cases, eleven presented the more marked changes

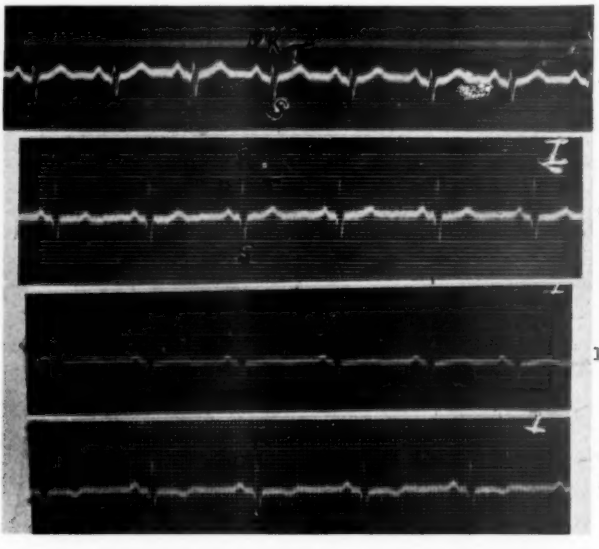


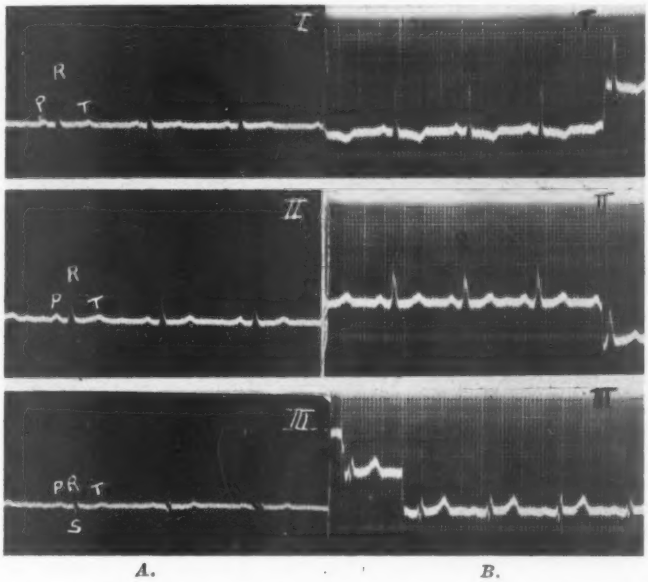
Fig. 11.—Lead I showing changes in the T-wave with depression and finally inversion after a period of three and one-half years. Anginal attacks began in 1924 but became more frequent and severe in 1927.

mentioned, definite aberrations of the QRS and inversion of the T-wave. In five cases the minor electrocardiographic alterations were present such as low voltage, lesser degrees of slurring and notching of the QRS or depression of the T-wave without inversion. Cases 6, 7, 8 and 9 are illustrative of extensive coronary disease showing the lesser degrees of abnormality in the electrocardiogram.

PRACTICAL APPLICATIONS

In the application of electrocardiography to the diagnosis of coronary disease, the following conception seems justifiable. The presence of T-wave inversion in significant leads or widened, notched QRS of bundle-branch or arborization block definitely indicates myocardial dis-

ease which, with some exceptions, is associated with coronary sclerosis. The chief exceptions, hypertension heart with a large dilated left ventricle, aortic valvular disease, the postdiphtheritic heart and myxedema heart, can be easily differentiated and excluded. In the absence of any symptoms or signs indicative of these conditions, as is especially true in Type 1 of coronary disease, the above-mentioned electrocardiographic changes can be considered as definitely diagnostic of coronary sclerosis. The lesser deviations of the electrocardiogram, low voltage, minor notchings and depressed T-wave, while not pathognomonic of coronary disease should not be disregarded. When the clinical picture is suggestive, the presence of these lesser changes should be con-



A. B.

Fig. 12.—(*A*). Leads I, II and III three months after the onset of typical anginal attacks. (*B*). T-wave in Lead I definitely inverted six months later.

sidered as additional support for the diagnosis of coronary disease. Especially in cases of depressed T-wave subsequent observation may reveal the development of a definite inversion (Figs. 11 and 12).

SUMMARY

From an analysis of the electrocardiographic findings in sixty cases of coronary sclerosis, T-wave inversion was found to be the most common abnormality, occurring in 88 per cent of the cases. Widened notched QRS was present in 13.3 per cent.

Attention is called to certain less definite changes such as minor notching of the QRS without widening and also low voltage. An attempt is made to evaluate the significance of these changes.

Increase in auriculoventricular conduction time was comparatively rare and found only associated with curves of bundle-branch block.

The most frequent arrhythmia was the extrasystolic type, which was present in 18 per cent. Auricular fibrillation was present in only 6.6 per cent and only in those cases showing evidence of congestive heart failure.

Preponderance curves of left ventricular type of definite or slight degree were noted in 60 per cent and slight right preponderance in only 3.3 per cent.

The presence or absence of cardiac enlargement or congestive heart failure seems to have little effect on the type of electrocardiogram.

A conception as to the practical application of electrocardiography in the diagnosis of coronary disease is suggested.

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THE CARDIAC RESPONSE IN ACUTE DIFFUSE GLOMERULONEPHRITIS*

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UNTIL recently, attention has been directed, almost exclusively, to the renal phases of acute diffuse glomerulonephritis. It has now, however, become generally recognized that simultaneously with the onset of acute glomerulitis there occurs a sudden rise in blood pressure. Despite the fact that this premise is well established, little attention seems to have been given to the symptoms which follow in its train. The importance and significance of the circulatory phenomena which usher in an attack of acute diffuse glomerulonephritis have not, in the writer's opinion, been sufficiently appreciated.

During the course of study of a series of cases of acute diffuse glomerulonephritis, with reference to the hypertension, it was noted that an unusual number of patients, though they presented unimportant renal symptoms, suffered from a circulatory disturbance. They were not always aware of any discomfort, the information being elicited by direct questions. It was also possible to suspect the presence of acute diffuse glomerulonephritis by a consideration of the mode of onset and the character of the circulatory decompensation, the diagnosis later being corroborated by the presence of hematuria, or urea retention in the blood.

The hypertension in this type of nephritis may be transient, lasting only a few hours. In the majority of cases, however, it persists for days or even weeks, depending upon the severity of the renal disease. Simultaneously with the advent of hypertension, circulatory symptoms appear. There may be dyspnea on exertion, so slight that it can scarcely be noticed by the patient. At times there is definite orthopnea which may cause but little subjective discomfort. In the recumbent position a definite increase in respirations may be observed; also a slight cyanosis around the lips. When told to sit up in bed, these patients acknowledge a sense of relief, previously not having recognized the cause of their discomfort.

In a second group of cases the circulatory symptoms are much more pronounced. The dyspnea is recognized by the patient as a "shortness of breath"; the orthopnea is more distressing, and he is aware of abdominal discomfort. Examination of the abdomen reveals an enlarged liver, often exceedingly tender. Coughing is a common symptom in this type of case. Crepitant and subcrepitant râles, often accompanied by sibilant breathing, are heard throughout the chest. This, with the

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presence of elevated temperature suggests a pulmonary basis for the trouble, but the true condition is finally revealed by a frank hematuria or some other characteristic symptom of acute nephritis.

In a third group of cases the cardiac symptoms predominate. Loud systolic murmurs are heard at the apex, often transmitted into the axilla; murmurs are also heard over the precordium. If the blood pressure has not been noted, or if the hypertension is transient, the basic pathological lesion may be overlooked, particularly if other renal symptoms are absent. On one occasion the writer saw a child, ten years old, with pulmonary edema and anuria, in whom the true cause of the trouble had not previously been recognized. The high blood urea nitrogen in this case disclosed the correct diagnosis.

The precipitant hypertension which follows the sudden onset of acute diffuse glomerulonephritis produces an unexpected strain upon the heart. The hypertension formerly was thought to be caused by an exudative inflammation in the glomeruli, which thus offered a mechanical obstruction to the flow of blood through the capillary tuft. Recently Volhard and Fahr have contended that the initial change in the kidney is a spasm of the afferent arterioles, producing anemia of the glomerular tuft, followed by exudative inflammation. Possibly, the arteriolar spasm is not confined to the kidney. This view seems to explain more clearly the sudden onset of hypertension. It is the sudden strain on the heart which causes it to yield. The gradual development of high blood pressure would never meet with such a response.

In the presence of so great a strain, the right chambers of the heart are the first to give way. The initial evidences of trouble are manifested in dilatation of the heart, congestion of the lungs, and a swollen liver. The heart, however, usually recovers promptly and the circulatory symptoms subside. This right sided decompensation may be so transient that often the symptoms are not apparent; usually they persist for days. On the other hand, if the pathological process in the kidney is intensive, the left side of the heart also yields, intensifying the symptoms of dyspnea and orthopnea, and in many instances leading to edema.

That the heart suffers in acute nephritis has not gone unmentioned in the writings of students of the subject. In 1879 Goodhart[1] wrote: "Probably many are quite alive to the occurrence of sudden death from ventricular dilatation in acute nephritis, but it is not taught as one of the things generally known." He reported five cases of acute scarlatinal nephritis, in four of which post-mortem examinations were performed. These showed dilatation of all cavities of the heart. In another case the right cavities only were dilated, and fatty degeneration of the cardiac muscle was observed. He attributed the cardiac failure to "sudden peripheral obstruction in the circulation and degenerative changes in the cardiac muscle." Later he added another case in which there was neither scarlet fever nor dropsy.[2] Clinically the area of

cardiac dullness was decidedly increased, and at post-mortem, acute nephritis and dilatation of both ventricles of the heart were found. He advised the use of digitalis in the treatment of such cases.

Silberman[3] described five cases in 1881, one terminating in pulmonary edema. Friedlander[4] made similar observations at autopsy. Steffen[5] described another case in which there were dyspnea and cyanosis. In 1889 Hutinel[6] taught that in the absence of cardiac disease, acute dilatation of the heart should be considered diagnostic of acute nephritis. He advised caffein therapy.

During the next twenty years no reference to the subject appeared in the literature, other than passing mention in several textbooks.[7, 8, 9] In 1909 Nobecourt and Voisin[10] described twelve cases of acute nephritis in children. Dilatation of the heart was invariably present. The clinical determination of the size of the heart was made by a percussion method described by Potain. In four of these cases recession of the area of cardiac dullness was found after recovery. These authors also believed with Hutinel that cardiac failure in the absence of a valvular lesion should be considered diagnostic of acute nephritis. Foucault[11] described thirteen similar cases in 1910.

In 1914 Volhard and Fahr[12] wrote a classical description of acute diffuse glomerulonephritis, noting the hypertension, edema, intense dyspnea and orthopnea, over-active heart beat, presystolic gallop, apical systolic murmur, accented apical first sound, diastolic apical thrust, displacement of the apex beat, and widening of the area of cardiac dullness. They stated that the cardiac response appeared greater in cases without edema, and that death could occur solely from pulmonary edema. Only two cases are cited. In 1917 Franeke[13] described dilatation of the heart in a series of sixty-nine cases of acute nephritis. Seventy-five per cent of the sixty-seven cases in which x-rays were available showed enlargement of the heart, which he considered to be a combination of hypertrophy and dilatation. Alwens and Moog[14] in 1920 described four cases with serial orthodiagrams showing enlargement of the heart and return to normal on recovery. They thought the enlargement due to acute dilatation and hydropericardium. Assmann[15] questioned this double etiology and both Goodhart and Volhard and Fahr had previously noted the presence of cardiac dilatation without the accumulation of fluid in the tissues and serous cavities.

Finally, Christian and O'Hare[16] in 1925 stated the contrary and entirely erroneous view. Their statement is categorical. "The heart is unchanged by acute nephritis except in a rare case." They further contend that enlargement of the heart or cardiac murmurs or arrythmias in acute nephritis should be regarded as coincident disturbances and that circulatory failure or a good response to cardiac treatment militates against the diagnosis. The weight of evidence is contrary to this opinion.

The physiology of cardiac enlargement in acute nephritis appears to have been best described by Goodhart whose explanation is given above. Volhard and Fahr hold a similar view. Wiggers[17] quotes adequate physiological experiments to confirm these clinical and pathological observations.

The response of the heart to an acute attack of glomerulo-nephritis is made apparent, not only by the circulatory symptoms encountered, but it may also be well visualized by teleroentgenograms. The sooner they are taken after the onset of the attack, the more successful will be the demonstration of acute cardiac dilatation. These facts will be illustrated in ten cases.

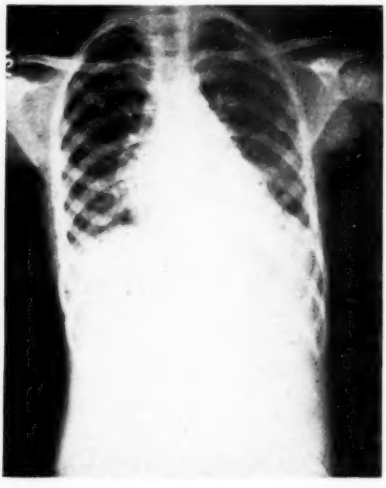

Fig. 1.—Case 1. Two days after onset of symptoms. Dilatation of the heart in all diameters. Congestion of pulmonic fields.

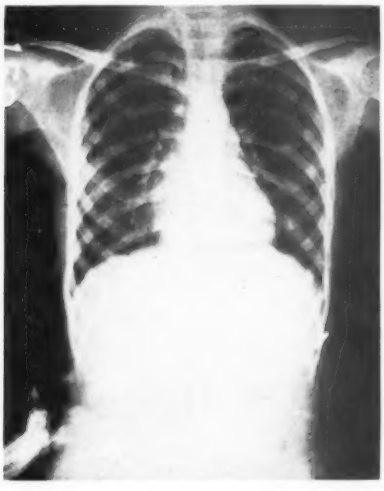

Fig. 2.—Case 1. Twenty-five days after onset of symptoms. Apparently normal in size and contour, but see Fig. 3.

CASE REPORTS

CASE 1.—Female, 8 years of age, was admitted to the City Hospital on May 7, 1924. The diagnosis was acute nephritis. Two days before admission she complained of "not feeling well," dyspnea and swelling of the face. The salient points in the physical examination were slight dyspnea, edema of the ankles and face and a loud systolic murmur at the apex of the heart. The blood pressure was 174 mm. systolic and 110 mm. diastolic. The urinary findings were characteristic; albumin, casts, and blood were found. The blood urea nitrogen was 35 mg. per 100 c.c. The child weighed 27 kg. (59.5 lbs.). The phthalein excretion was 40 per cent in the first hour and 30 per cent in the second. She was put to bed without any special medication on a diet consisting of 1500 calories and 25 grams of protein.

At the end of three weeks there was a definite improvement in her clinical condition. The blood urea nitrogen was normal, but the urine still contained blood. The protein in the diet was then increased to 40 grams, and in a few days there was a definite increase in the level of the blood urea nitrogen to 26 mg. per 100 c.c. Again placed on a 25 gram protein diet the nitrogen level in the blood fell to

normal. Later, an increase of the protein to 35 grams produced no increase in the nitrogen level in the blood. She was discharged June 30, apparently normal.

In a few months she was requested to return and was again admitted on September 15. The only positive finding on this date was a trace of albumin in the urine. On a diet containing over 50 grams of protein, no rise in the urea content of the blood occurred.

The first teleroentgenorgram (Fig. 1) was taken two days after the onset of symptoms. It shows the heart dilated in all diameters, more particularly to the right, borders indistinct, and merging into the congested pulmonic fields.

The second teleroentgenogram (Fig. 2) was taken twenty-three days later. At this date all her symptoms had disappeared and the nitrogen content of the blood was normal on a 25 gram protein diet. The blood pressure was normal, and only a slight trace of albumin, but no blood cells were found in the urine. In this teleroentgenogram there is a resumption of the diameters of the child's heart toward normal figures; in fact at this time the heart was regarded as being

Fig. 3.—Case 1. Three months later. Normal size and contour.

normal in size and contour. The following facts, however, suggested that the pathological process in the kidney was not absolutely healed. When placed on a 40 gram protein diet, the blood pressure and the urea-nitrogen level in the blood were raised, within four days. With a return to the 25 gram protein diet both blood pressure and blood nitrogen returned to normal.

The third teleroentgenogram (Fig. 3) was taken four months after the onset of symptoms. At this date a clinical and metabolic survey of the case suggested complete healing of the renal process. Examination of the plate shows that the diameters of the heart are smaller than on the previous examination, representing the absolute normal size and contour for a child of her age and size. From this we learned that the second teleroentgenogram (Fig. 2) was erroneously interpreted as showing a normal-sized heart. It should be noted that at that time, although the patient's blood pressure at rest was normal, other evidence indicated that the renal process was not healed.

Case 2.—Male, 38 years of age, was admitted to the dermatological service of the City Hospital for an eruption due to pediculosis. He had scarlet fever at the

age of 8 years, at which time he was told he could never be perfectly normal. In 1917 he had influenza with fever and cough. Subsequently he developed a winter cough.

Six weeks after admission a generalized edema developed and he was transferred to the medical service and later to the metabolic service on February 26, 1927. Examination early in February revealed the following facts. He was dyspneic. No murmurs were heard. The blood pressure was 140 mm. systolic and 90 mm. diastolic. Coarse râles were heard over the whole chest posteriorly. On close questioning it was learned that he had noticed some dyspnea on exertion for two and one-half weeks previously. When transferred to the metabolic service he was dyspneic and acutely ill. He weighed 85 kg. (187 lbs.). The urine contained albumin, hyaline, and granular casts and blood. The blood urea nitrogen was 31 mg. per 100 c.c. On the administration of diuretin and a diet containing 25 grams of protein he improved clinically in a short time. He was kept on this diet for about seven weeks, and small doses of digitalis were also given. The blood urea-nitrogen level returned to normal. He lost 20 kg. (44 lbs.). The protein in the diet was increased to 40

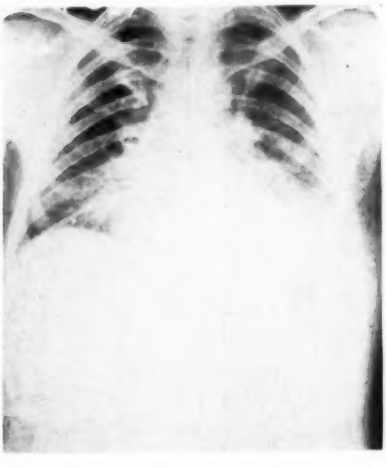

Fig. 4.—Case 2. About three weeks after onset of symptoms. Dilatation of the heart in all diameters. Congestion of pulmonic fields.

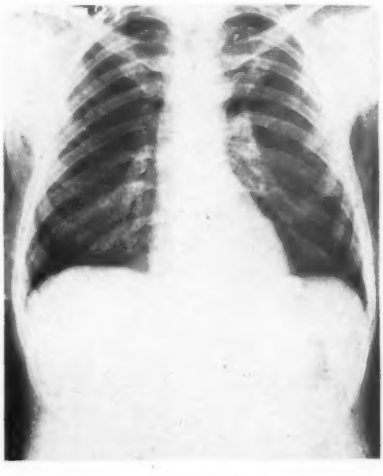

Fig. 5.—Case 2. Three months later. Normal size and contour.

grams and then to 60 grams, both of which were well tolerated. He was discharged May 4, 1927, and took a position as orderly in the hospital.

The first teleroentgenogram (Fig. 4) was taken about three weeks after the appearance of the first symptoms. The heart was dilated enormously in all diameters, with obliteration of the right costophrenic sinus and marked congestion of the lungs. A teleroentgenogram taken three months later shows an unusual transformation (Fig. 5).

Case 3.—Male, 38 years of age, was admitted to Bellevue Hospital on February 22, 1927, for erysipelas of the face and legs. One week later he was discharged as cured. Four days after this he noticed swelling of the legs, ankles and face. He had a slight cough and complained of indigestion. Returning to Bellevue Hospital he was later transferred to the City Hospital and admitted to the metabolic service on April 12.

The heart was apparently normal. The blood pressure was 120 mm. systolic and 80 mm. diastolic. The urine contained albumin and blood. The blood urea nitrogen

was 28 mg. per 100 c.c. He was given a 25 gram protein diet for four weeks. The blood urea nitrogen at the end of this time was 17 mg. per 100 c.c. The diet was increased to 40 grams of protein, then to 60 grams, and finally to 100 grams, which was tolerated very well. He was discharged in good health.

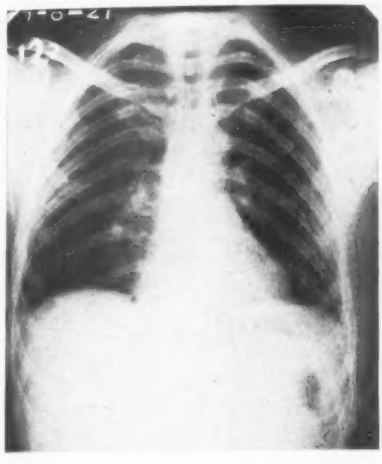

Fig. 6.—Case 3. One month after onset of symptoms. Maximum right horizontal diameter 4.6 cm. Maximum left horizontal diameter 10.3 cm. Pulmonic fields 30 cm.

Fig. 7.—Case 3. Thirteen days later. Slight reduction in size of heart. Maximum right horizontal diameter 4 cm. Maximum left horizontal diameter 9.3 cm. Pulmonic fields 30 cm.

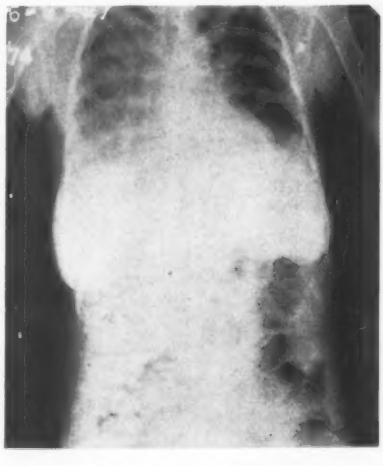

Fig. 8.—Case 4. Six days after onset of symptoms. Dilatation of heart in all diameters. Congestion of pulmonic fields.

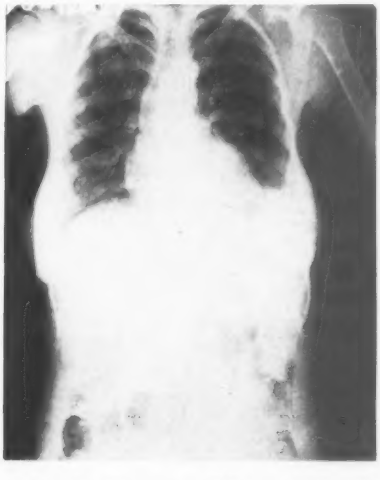

Fig. 9.—Case 4. Fifteen days after onset of symptoms. Slight decrease in size of heart. Borders distinct. Pulmonic fields clear.

The first teleroentgenogram (Fig. 6) was taken one month after the onset of symptoms. Two weeks later when his blood pressure was normal and when there were no red blood cells in the urine and the patient appeared clinically well, the second teleroentgenogram (Fig. 7) was taken. It shows a reduction, though slight, in the size of the heart, from which it must be concluded that even one month

after the onset of symptoms the heart had not returned to its normal size. This indicates that the size of the heart may be an index to the progress of the renal pathology.

CASE 4.—Female, 20 years old, fainted while going to work. She had felt a "shortness of breath" for a few days prior to this. Two days later she was admitted to the hospital. There was a blowing systolic murmur at the apex of the heart. The blood pressure was 190 mm. systolic and 130 mm. diastolic. There were a few crackling râles at the bases of the lungs. The liver was percussed to three fingers below the costal margin and was tender. The extremities were not edematous. Although the urine contained albumin, there were no red blood cells. The blood urea nitrogen was 40 mg. per 100 c.c. She was placed on a 25 gram protein diet. At the end of one week the blood urea nitrogen fell to 24 mg. per 100 c.c. The blood pressure decreased to 150 mm. systolic and 100 mm. diastolic. During the following week she insisted on being discharged.

The first teleroentgenogram (Fig. 8) was taken six days after the appearance of symptoms. It shows the usual cardiac dilatation and pulmonic congestion. The

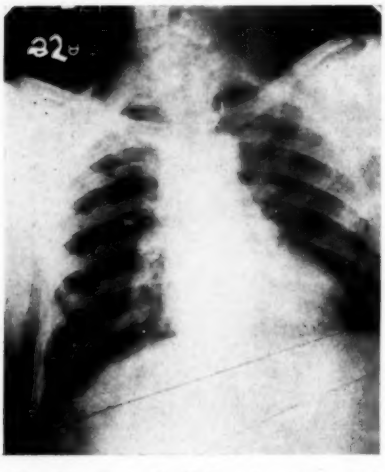

Fig. 10.—Case 5. Taken in prone position at less than six feet distance from target. Three weeks after onset of symptoms. Bronchopneumonia in right upper lobe. Dilatation of the heart.

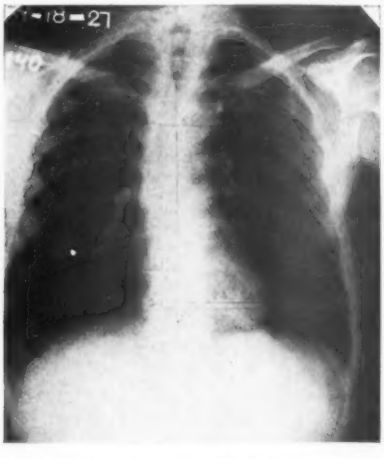

Fig. 11.—Case 5. Usual technic for teleroentgenogram. Six days later. Heart normal in size and contour.

second teleroentgenogram (Fig. 9) was taken nine days after the first. The heart is reduced in size although not normal, and the pulmonic fields are considerably clearer. At this time although the patient was symptom-free, the blood pressure was still elevated. That the renal lesion was not entirely healed is shown by the failure of the cardiac shadow to return to normal dimensions and contour, as well as by the hypertension and disturbance of the nitrogen metabolism.

CASE 5.—Male, 51 years old, was admitted to the medical service on April 10, 1927. He was in good health until about three weeks before admission when he complained of dyspnea. His chief complaints, however, were generalized aches and pains throughout the body. Physical examination showed enlargement of the heart to the left, a loud systolic murmur at the apex of the heart, and blood pressure 140 mm. systolic, 90 mm. diastolic. The liver was enlarged and tender, and the legs slightly edematous. The physical signs in the chest were such as to suggest a diagnosis of confluent bronchopneumonia. The temperature fluctuated between 101° and 103° F. There were albumin, casts and blood in the urine.

Large doses of caffein were administrated for nine days, at which time he was seized with general convulsions. It was questionable whether these were due to the caffein administered or to uremia.

On April 19, 1927, the patient was transferred to the metabolic service. Within a few days, although the dyspnea subsided, the blood urea nitrogen gradually increased to 64 mg. per 100 c.c. He began to show signs of chronic uremia. Treatment was with forced fluids and a negligible nitrogen intake. After several days the blood urea nitrogen decreased and clinical improvement was evident. He received a 25 gram protein diet for about five weeks, the blood urea nitrogen falling to 18 mg. per 100 c.c. The diet was then increased to 60 grams of protein and finally to 80 grams, this amount of nitrogen being fairly well borne.

The first roentgenogram (Fig. 10) was taken about three weeks after the onset of symptoms. Unfortunately it was a chest plate. It shows a suspicious patch of bronchopneumonia in the right upper lobe and a dilated heart.

A teleroentgenogram (Fig. 11) was taken one week later. Although these two roentgenograms are not absolutely comparable, there is little question that the

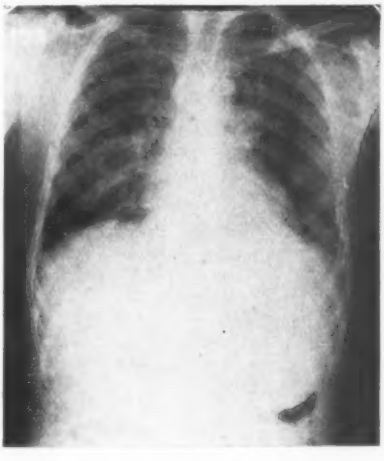

Fig. 12.—Case 7. Ten days after onset of symptoms. Maximum right horizontal diameter 4.5 cm. Maximum left horizontal diameter 9.9 cm. Pulmonic fields 26.8 cm.

heart was definitely dilated at the time of the first and that in one week it had resumed its normal size and contour. To bring about similar changes in other cases required a much longer period, and it is our impression that in this case the free use of caffein was responsible for the excellent results achieved.

Case 6.—Male, 22 years old, was in a hospital for one month in 1918 because of "grippe." He worked until September, 1926, when he had an attack of pleurisy and pneumonia. Three weeks later his ankles were swollen, and later the edema involved the entire body. He did not have dyspnea. He entered Bellevue Hospital when he discovered blood in his urine. Within six weeks the edema had disappeared but he was anemic. A blood transfusion was followed by a severe reaction.

He was admitted to the metabolic service of City Hospital on March 5, 1927. Examination revealed anemia, slight edema of the extremities, a blood pressure of 150 mm. systolic and 90 mm. diastolic. The urine contained blood. The urea nitrogen of the blood was 31 mg. per 100 c.c. He was put to bed, given the usual medication and a 25 gram protein diet, the latter being continued for several

weeks until the blood urea nitrogen was normal. The diet was increased to 40 grams of protein, but every attempt to further increase the protein content of the diet met with an increase of blood urea nitrogen to above normal figures. He felt much better but there was little improvement in the anemia.

The first teleroentgenogram was taken about six months after the appearance of the initial symptoms. Two months later very little change in size and contour was found. This suggests that during the period from the onset of symptoms until his admission to the metabolic service he had completely recovered from the acute circulatory decompensation, although he was suffering with the outstanding symptoms of chronic glomerulonephritis.

CASE 7.—Male, 24 years old, was admitted to the nose and throat service of the City Hospital for recurrent epistaxis which had persisted intermittently for ten days. On close questioning he admitted that during this period he was dyspneic and had slight edema of the extremities. His face was pallid. A systolic murmur was heard at the apex of the heart. Both pulmonary bases were

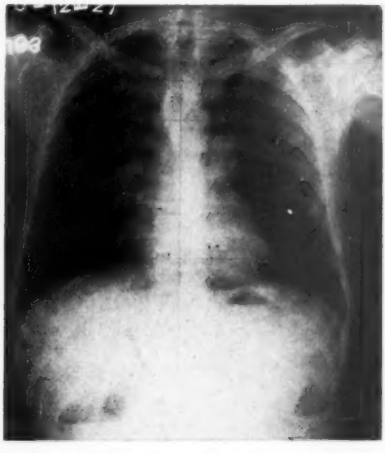

Fig. 13.—Case 7. Three weeks later. Maximum right horizontal diameter 4 cm. Maximum left horizontal diameter 8.4 cm. Pulmonic fields 27.9 cm.

filled with numerous râles, and the breath sounds throughout the lungs were sibilant. The liver could be percussed to three fingers below the costal margin but was not tender. The fundus was normal. The urine contained granular and hyaline casts and blood. The blood urea nitrogen was 88 mg. per 100 c.c. The blood count revealed an anemia and leucocytosis, viz., hemoglobin 45 per cent, R.B.C. 3,250,000, W.B.C. 13,800. The blood pressure was 150 mm. systolic and 80 mm. diastolic. He was transferred to the metabolic service on May 5, 1927, given the usual medication and a 25 gram protein diet for about four weeks. The blood urea nitrogen diminished to within normal limits, and the diet was accordingly increased to 60 grams of protein and finally to 80 grams with no retention of nitrogen in the blood.

The first teleroentgenogram (Fig. 12) was taken ten days after the onset of symptoms. It shows the usual dilated heart. One taken almost three weeks later demonstrated that the heart had returned to its normal size and contour (Fig. 13). The patient at this date had not entirely recovered. The urea-nitrogen level in the blood was slightly elevated on a 25 gram protein diet, although the urine was normal.

CASE 8.—Male, 49 years old, was admitted to the medical service because of dyspnea and orthopnea. He was in great distress. The diagnosis was general arteriosclerosis and cardiac decompensation. An outstanding feature of the case was the enlargement and tenderness of the liver. The urine contained albumin, a few granular casts and many pus cells. Two days after admission the blood urea nitrogen was 12 mg. per 100 c.c. Nine days later it was 23 mg. per 100 c.c. He died within one month with all the symptoms of circulatory decompensation.

Post-mortem Examination: The heart weighed 670 grams and showed evidence of chronic myocarditis. The left ventricle was thickened, the right ventricle and auricle were enormously dilated. The coronary arteries and heart valves were normal. The kidneys each weighed 300 grams. The line of demarcation between cortex and medulla was absent. Histological examination of the kidney revealed arteriosclerosis and acute diffuse glomerulonephritis.

The teleroentgenogram (Fig. 14) shows a heart dilated enormously in all diameters, particularly to the right. The interesting feature of this case is the presence of acute glomerulonephritis without definite evidence in the urine or blood.

Fig. 14.—Case 8. Dilatation of the heart in all diameters.

The acute dilatation of the heart, particularly to the right, and the large and tender liver, without any endocardial, pericardial or coronary cause, should have led one to suspect that the basis of this acute dilatation was acute nephritis.

CASE 9.—Male, 39 years old, was admitted to the medical service about two weeks after the onset of symptoms. He complained of pain in the legs and abdomen and of shortness of breath for ten days. Then he noticed edema of the extremities. Physical examination revealed general anasarca, a systolic murmur at the apex of the heart and absence of breath sounds at the bases of the lungs. The blood pressure was 270 mm. systolic and 120 mm. diastolic. Scattered throughout both retinas were numerous hemorrhages and a few white exudative areas. The margins of the optic discs were fairly sharp. The blood urea nitrogen was 40 mg. per 100 c.c. The urine contained blood. Under the usual medical and dietetic régime he improved greatly. The blood pressure dropped to 128 mm. systolic, the body weight decreased 15 kg. (33 lbs.), and the urine was free of blood.

The first teleroentgenogram was taken two weeks after the onset of symptoms. The second taken two weeks later shows a slight but appreciable change.

CASE 10.—Female, 19 years old, came to my office June 16, 1924, complaining of puffiness of the legs and face which was noticed the previous day. She had had an aching precordial pain for two days, although there was neither dyspnea nor palpitation. Two weeks previously she had an attack of follicular tonsillitis and developed a cough but gradually improved. The heart was slightly overactive but otherwise negative. The blood pressure was 115 mm. systolic, 80 mm. diastolic. The liver was palpable three fingers below the costal margin and distinctly tender. The lungs were not congested. The fundus was normal. The urine showed a trace of albumin, granular and hyaline casts and several red and white blood cells to each microscopic field. The blood urea nitrogen was elevated; 52 mg. per

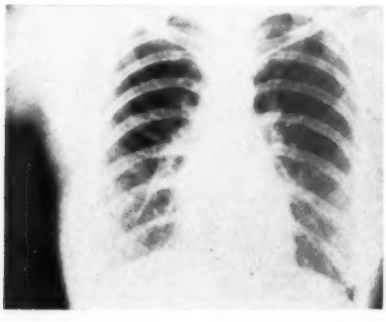

Fig. 15.—Case 10. Two days after onset of symptoms. Maximum right horizontal diameter 4.3 cm. Maximum left horizontal diameter 6.7 cm. Pulmonic fields 24.5 cm.

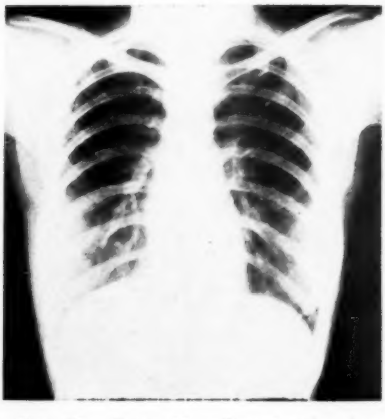

Fig. 16.—Case 10. Twenty-six days after onset of symptoms. Maximum right horizontal diameter 3.3 cm. Maximum left horizontal diameter 5.5 cm. Pulmonic fields 24.5 cm.

Fig. 17.—Case 10. Almost three years later. Maximum right horizontal diameter 4.6 cm. Maximum left horizontal diameter 6 cm. Pulmonic fields 25 cm.

100 c.c. Although the patient felt no discomfort, she appeared dyspneic. She was sent home and put to bed for three weeks on the usual medication and dietetic treatment, she improved greatly. On July 10 the urine was normal. The blood urea nitrogen was 19 mg. per 100 c.c. The blood pressure was 100 mm. systolic and 60 mm. diastolic.

After an interval of almost three years she again presented herself for examination, stating that she had slight pain over her heart when tired. No abnormalities were found on physical examination.

A teleroentgenogram (Fig. 15) taken two days after the onset of the circulatory symptoms demonstrated the dilatation of the heart in all diameters, particularly to the right. It should be noted that at this date her blood pressure was normal. A teleroentgenogram (Fig. 16) taken after all symptoms had subsided showed the heart practically normal in size and contour for a girl of her physique. The third teleroentgenogram (Fig. 17) taken almost three years later showed the heart to be definitely larger than in 1924.

There are several interesting features in this case. Although the patient was undoubtedly suffering with acute glomerulonephritis and showed a dilated heart in the teleroentgenogram, her blood pressure was not elevated. The interpretation of the cardiac enlargement three years later is not a simple matter. It may have been due to the normal growth of the heart in a girl who had advanced three years in age and over twenty pounds in weight, or it may have been the result of a latent chronic glomerulonephritis which presented no other symptomatology.

I am unable to present any conclusive data as to the electrocardiographic abnormalities in acute nephritis.*

SUMMARY

The recognition of the presence of acute circulatory decompensation is extremely important in the diagnosis and treatment of acute diffuse glomerulonephritis. The cardinal symptoms, namely, hypertension, edema, hematuria and renal insufficiency as shown by nitrogen retention in the blood, may be absent. The pathology in the kidney consequently may not be detected. Cases of this description are reported in this series. The only clue to the diagnosis is obtained by a proper interpretation of the circulatory symptoms. The sudden advent of circulatory decompensation as evidenced by dilatation of the right side of the heart, pulmonary congestion, and an enlarged and tender liver should lead one to suspect the presence of acute nephritis. This applies particularly in cases in which valvular or coronary artery lesions are absent and no other cause for decompensation can be found. Although it is generally believed that the edema in acute diffuse glomerulonephritis is a "tissue disturbance," caused by some derangement of general metabolism, the fact must not be overlooked that water retention may also be due to the circulatory disturbance. The determination of this point is of extreme importance in deciding upon the form of therapy to be pursued. Pulmonary edema may be the cause of death in acute nephritis. It may occur even though the structural changes in the kidney are not sufficient to produce complete renal insufficiency. The early recognition of the etiology of the circulatory symptoms may be the means of saving life. In addition to dietetic measures, proper cardiac supportive treatment should be undertaken. Often, rest in bed will suffice. The liberal use of caffein products such as diuretin, theocalcin and caffein sodium benzoate, and digitalis are indicated.

*Electrocardiograms were taken in seven of these ten cases. In three (Cases 2, 5 and 6) there are no significant abnormalities. In one case (Case 10) the T-wave is unusually high and pointed in Leads I and II. In the remaining three cases (Cases 4, 8 and 9) inversion, diphasic character or flattening of the T-waves in Leads I and II are present, but all had received some digitalis. Other cases seem to indicate the presence of abnormalities of the T-wave in some stage of the disease.

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CHARACTERISTIC ELECTROCARDIOGRAMS AND ROENTGENOGRAMS IN ARTERIAL HYPERTENSION

Their Prognostic Significance*

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THE electrocardiographic and roentgenographic changes in patients with arterial hypertension have been found to be so characteristic and their relations to the clinical findings of such prognostic value that it has been deemed advisable to report them. When one considers that an individual may have marked hypertension for from twelve to fifteen years before developing definite symptoms of myocardial failure, any aid to prognosis, such as the electrocardiogram and the roentgenogram, is of value. Fahr[1] and others have recently emphasized the prevalence and chronicity of hypertension.

The 152 patients studied† were those with blood pressures habitually above 160 mm. systolic, and 90 mm. diastolic. By far the greater number had essential hypertension, only 10 per cent were associated with nephritis. The data cover a period of at least three years and a follow-up system has kept the records up to date. One or more electrocardiograms were taken in every case and in 106 patients, one or more teleroentgenograms.

Ninety-two of the patients were females and 60 were males. The ages ranged from eleven to eighty years; 18 patients were under forty, 29 patients were between forty and fifty, 50 patients were between fifty and sixty, 28 patients were between sixty and seventy years of age.

The literature on the electrocardiographic changes in hypertension is very meager. Einthoven[2] noted an inversion of the main deflection of the QRS group in the third lead in patients with hypertrophy of the left ventricle. Linetzky[3] was the first to study the effect of high blood pressure on the electrocardiogram. He discovered that with an augmentation in blood pressure the R-wave increased in amplitude while the T-wave diminished. He stated that the T-wave was usually negative in patients with a systolic blood pressure over 230 mm. His belief was that hypertension caused an enlarged heart and that the latter produced these electrocardiographic changes. Lewis,[4] in 1913, concluded that "high blood pressure appears to be especially potent in creating a preponderance of the left ventricle." Munk[5] mentioned tall R-waves, negative T-waves in Lead I, premature beats and auricu-

*Read before the Section on Internal Medicine, New York Academy of Medicine, March 19, 1929.

†Through the courtesy of Dr. B. S. Oppenheimer of New York, the data here presented were taken for the most part from his private records. In about ten cases the records of Mount Sinai Hospital, New York, were also utilized.

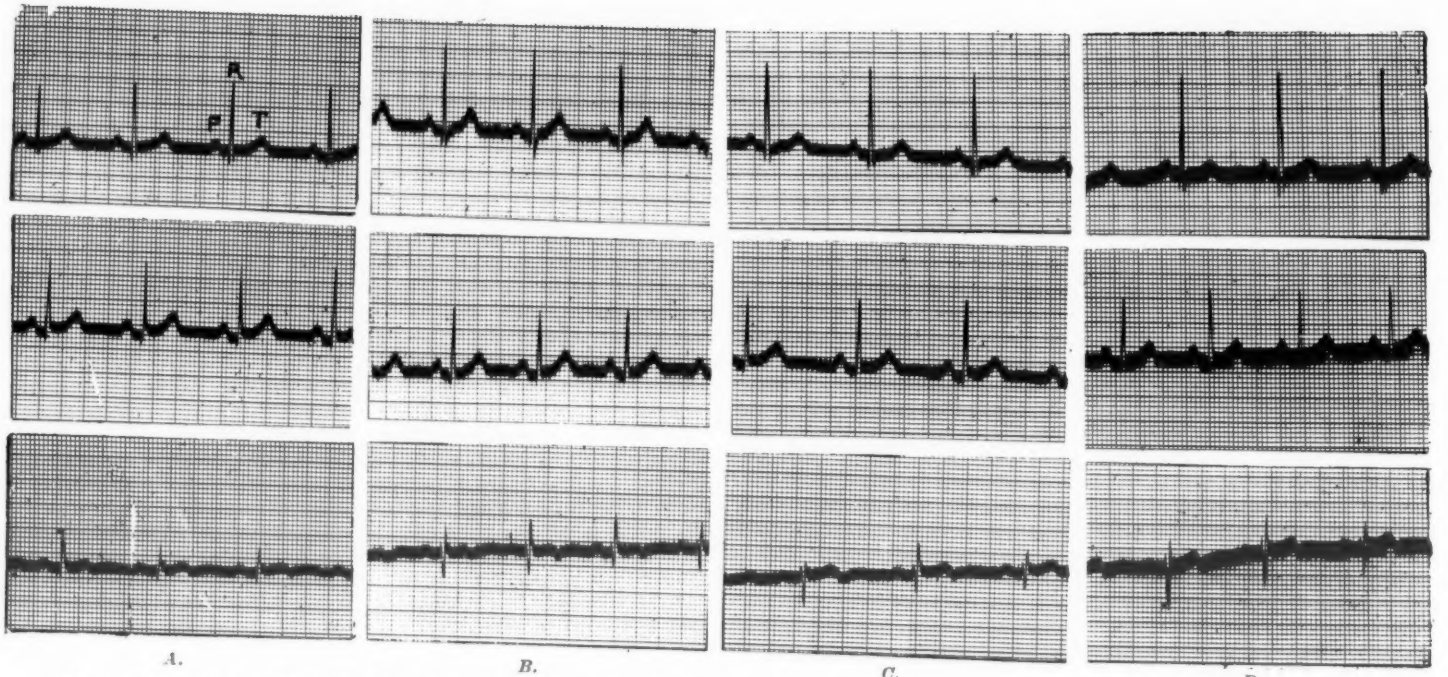

Fig. 1.—*A*, Dec. 23, 1921. Normal electrocardiogram. Age of patient fifty-nine years; *B*, Mar. 8, 1923. Blood pressure 150/90. Development of a moderate left axis deviation. Increase in amplitude of R- and S-waves; *C*, Dec. 29, 1923. Blood pressure 152/90. More definite left axis deviation; *D*, Oct. 26, 1925. Blood pressure 200/90. Further increase in voltage of QRS group; *E*, Nov. 10, 1927. Blood pressure 170/100. T-wave in Lead I flat (isoelectric); *F*, Mar. 25, 1928. Blood pressure 178/100. Further increase in voltage of QRS group. T-wave in Lead I slightly inverted; *G*, Nov. 1, 1928. Blood pressure 174/104. T-wave in Lead I definitely inverted.

lar fibrillation as occurring in hypertension. White and Burwell[6] studied unselected cases of hypertension and found from 44 to 47 per cent of the patients to have left axis deviation of the QRS group, i.e., a left ventricular preponderance. Their percentages were smaller than my own.

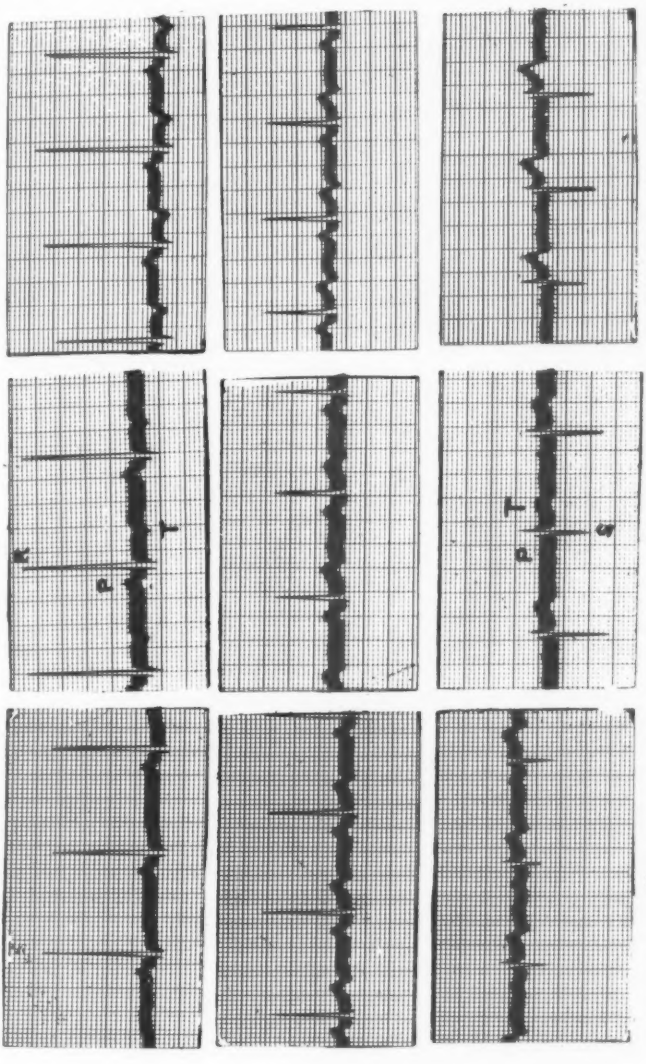

Fig. 1.—Cont'd

ELECTROCARDIOGRAPHIC STUDIES

The most common change found was that of the left axis deviation. This was present in 112 persons out of a total of 152, i.e., 74 per cent (Fig. 1, *C, D, E, F, G*). This is a decided increase over normal figures in the same age groups, and constitutes, therefore, a definite electrocardiographic finding in hypertension cases. Twenty-three of these

patients died, a percentage of 21, whereas the general mortality rate of all the patients for three years was 18 per cent.

The second most common finding was a combination of left axis deviation with inversion of the T-wave in Lead I (Fig. 1, *G*). This occurred in 36 per cent of the cases. The serious import of the inverted T-wave is readily appreciated when its frequent association with coronary artery disease and myocardial involvement is recalled. The mortality rate in this group was 27 per cent. Every case of T-wave inversion in the first lead was associated with a left axis deviation of the QRS group.

The third most common change seen in the electrocardiograms of hypertension patients was a combination of high voltage of the QRS group, a left axis deviation, inversion of the T-wave in the first lead, and shortening or disappearance of the R-T or S-T intervals (Fig. 1, *G*). The amplitude of the waves of the QRS group is usually 18 millimeters or more in at least one lead. The duration of the QRS waves is usually within the normal limits, i.e., 0.10 second, but 0.12 second in a case with high voltage must be considered normal. In general the T-waves are directed oppositely to the main deflection. For descriptive purposes this type of record has been called the high-voltage electrocardiogram in hypertension.

The development of the high-voltage electrocardiogram is gradual, and is related rather to the duration of the hypertension than to the height of the blood pressure. Fig. 1 illustrates the case of a woman now sixty-seven years of age who has had hypertension for at least eight years. The normal record gradually changes to a left axis deviation, then there occurs an increase in voltage of the QRS group with development of inversion of the T-waves in the first and second leads. The R or S-T interval shortens or disappears entirely.

All patients in the "high voltage" group who have had numerous electrocardiographic tracings showed changes over a period of years. Fourteen patients were followed from two to nine years. When the investigation was conducted over a sufficient period of time and if records were taken frequently enough, every one of these changes was usually noted; at other times there occurred a change from a normal tracing to one with a left axis deviation, a change from a normal voltage of the R- and S-waves to one of high voltage, or from an upright T to an inverted, or a combination of all of these.

The high-voltage electrocardiogram in hypertension occurred in 33 patients. The mortality among these was very high—40 per cent for three years.

Twenty-six of these patients were roentgenographed. Sixteen of these showed a dilated ascending aorta and 24 showed evidences of a definite concentric hypertrophy of the left ventricle. In other words

the high-voltage electrocardiogram in hypertension is associated with the x-ray changes usually seen in hypertension.

ROENTGENOGRAPHIC STUDIES

Coincidentally with the electrocardiograms, teleroentgenograms were taken on 106 patients.

Munk[5] and Vaquez and Bordet[7] have described the heart in hypertension. They speak of an elongated, tortuous aorta, of a left ventricle that is hypertrophied, and of a heart in which the longitudinal

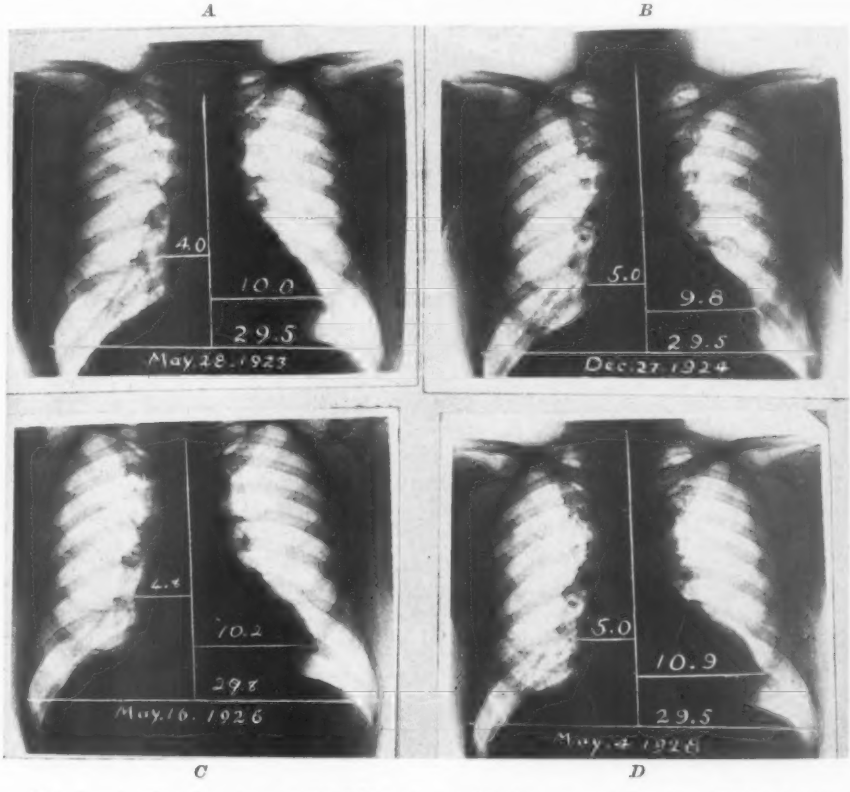

Fig. 2.—*A*, Blood pressure 158/100. A practically normal heart. (Slight hypertrophy of left ventricle); *B*, Blood pressure 166/100. Heart enlarged. Left ventricular hypertrophy. Tortuous aorta, prominent aortic knob. *C*, Blood pressure 160/100. A further left ventricular hypertrophy. *D*, Blood pressure 170/110. A marked left ventricular hypertrophy with rounded apex.

and transverse diameters may become considerably increased. Munk gives diagrammatic illustrations of changes in the aorta and left ventricle.

The habitus of this group was also studied. The criteria here used are those proposed by Groedel,[8] and Hirsch and Shapiro.[9] Six patients belonged to the hypersthenic, 77 to the sthenic, and 23 to the hyposthenic type. It is usually the sthenic or hypersthenic type of individual that develops hypertension.

The left ventricle was hypertrophied and more or less sharply outlined in at least 48 per cent of the cases. This fact added no prognostic significance to the clinical history. A left ventricle hypertrophy by x-ray film was usually associated with a left axis deviation by the electrocardiogram, but a left axis deviation did not necessarily indicate a hypertrophy of the muscle chamber, as seen in the x-ray picture.

The shadow of the ascending aorta was definitely widened (Figs. 2 and 3) in 23 patients, and slightly widened in 11 more. The mortality among these patients was slightly higher than the average—22 per cent for the three years. This dilatation of the aorta is more apparent than real in that the vessel which appears somewhat to the right can be shown by fluoroscopy or by sagittal-view roentgenogram to be tortuous rather than dilated. Munk[5] and Vaquez and Bordet[7] have called attention to this point.

The hypertension roentgenogram is characterized by the sthenic or hypersthenic type of chest, the hypertrophied left ventricle, the

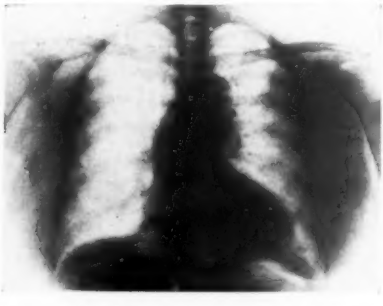

Fig. 3.—Tortuous aorta. Aortic knob prominent. Left ventricular hypertrophy.

enlarged heart, the dilated or tortuous aorta, and the prominent aortic knob (Figs. 2, *C*, *D*, and 3). These late changes in the heart and aorta are indicative of a previous long-standing hypertension. Fig. 2 shows the progressive changes in the size, shape, and position of the heart and aorta in a case of chronic hypertension, beginning with a practically normal heart.

DISCUSSION

The explanation of the three common electrocardiographic findings in hypertension, namely, (1) left axis deviation, (2) left axis deviation with the T-wave inversion in the first lead, and (3) the high-voltage electrocardiogram in hypertension, probably lies in the size, shape, and position of the left ventricle, or, more accurately, in the length and direction of the specific conduction pathways. Cohn[10] in experiments on human beings, and Meek and Wilson[11] in experiments on dogs, have shown that change in position and rotation of the heart may alter the axis deviation and transform a positive T-wave into a negative one. The time relations, i.e., the onset of excitation of the

bundle branches; the length and direction of this excitation in each bundle branch, and the change, if any, in the time of retreat of the conduction wave or in its direction, are all important factors with respect to the fixed leads.

When one considers specifically the inversion of the T-wave, the same explanation is at hand, but the possibility of coronary artery disease must be considered. Patients with hypertension often have coronary artery involvement. At post-mortem examination these vessels may be found to be markedly diseased. However, the previous explanations may nevertheless hold true, for a coronary artery occlusion with its resultant thrombosis probably throws out of balance the electrical pathways of the right and left ventricles. Moreover, it has been suggested that following a closure, a change in size, shape, and rotation of the left ventricle may account for the inverted T-wave.[12] Luten and Grove[13] believe that records with a left axis deviation, inversion of the T-wave in Lead I and normal QRS groups are caused by defective conduction in the right limb of the A-V bundle and that this defective conduction is due to disease of the left coronary artery. The evidence at hand, however, tends to show that if hypertension in a patient with the high-voltage electrocardiogram persists long enough, the T-wave will eventually become inverted and remain so, whether or not coronary artery disease be present. Again, this typical electrocardiogram, with the marked left axis deviation and inversion of the T-wave in Lead I, is very occasionally seen in young children with a pure aortic insufficiency of rheumatic origin where there is no question of coronary artery disease. Moreover, the T-wave of the high-voltage record is deeper and narrower than that of the inverted T of the ordinary coronary artery closure case. Finally, it seems that once this T-wave becomes inverted it remains so, whereas in recovery from a closure of the coronary artery the patient is apt to lost the negativity of his T-wave.

The high-voltage electrocardiogram in hypertension, as described in this paper, was first called the "hypertension electrocardiogram"[14] but the use of this term is open to criticism since these electrocardiographic changes have occasionally been seen in uncomplicated cases of aortic insufficiency.

It must be emphasized that not every patient with hypertension will show either this high-voltage electrocardiogram or the hypertension x-ray picture. The converse is true nevertheless, that these graphic changes, if present in a patient who has no aortic insufficiency, indicate that the patient must have had arterial hypertension for many years.

High voltage of the QRS group alone, i.e., with no T-wave inversion, was not included among the significant changes, although it is believed

that the positive T-wave ultimately becomes inverted. It is probably an early stage of the high-voltage electrocardiogram in hypertension.

A word must be said of the possible clinical significance of the high-voltage record as well as the hypertension roentgenogram. I believe that they indicate a long-standing hypertension even when there is no history or current clinical evidence of it. Such an electrocardiogram has been seen in patients with coronary artery disease who have lost their hypertension. A clinical study is at present being made of patients who yield these high-voltage electrocardiograms, and it seems probable that these records may give as much evidence to the clinician of a previous long-standing hypertension as does the hypertrophied left ventricle at the autopsy table to the pathologist.

SUMMARY

The electrocardiographic and teleroentgenographic records of 152 patients with hypertension have been studied. The general mortality among these patients, covering a follow-up of three years, was 18 per cent.

Seventy-four per cent of the patients showed left axis deviation in the electrocardiogram. This is therefore a common change in hypertension cases. However, it does not necessarily indicate a left ventricular hypertrophy by x-ray picture.

The next most common finding was a combination of left axis deviation with T-wave inversion in the first lead. This occurred in 36 per cent of the cases. The mortality rate in this group was 27 per cent.

Every case of T-wave inversion in the first lead was associated with left axis deviation.

The high-voltage electrocardiogram in hypertension was present in 22 per cent of all the cases. Among these patients the mortality was high—40 per cent. This electrocardiogram, when pure aortic insufficiency is not present, appears to be characteristic of long-standing hypertension. A gradual change in the size, shape, and position of the left ventricle probably accounts for the electrocardiographic findings.

Of 106 patients in whom teleroentgenograms were taken, 78 per cent belonged to the so-called sthenic or hypersthenic types of habitus.

The hypertension roentgenogram, characteristic of long-standing hypertension, shows an enlarged heart, an hypertrophied left ventricle, and an apparently dilated but actually tortuous aorta, with a prominent aortic knob.

The left ventricle appeared hypertrophied on the roentgenogram in 48 per cent of the patients. In each case a left axis deviation was present in the electrocardiogram.

The ascending aorta was apparently widened in 32 per cent of the cases. Accurately speaking the aorta is not widened but is tortuous.

The "high-voltage electrocardiogram" or the "hypertension roentgenogram" may be the only existing evidence of a previously long-standing hypertension.

I wish to express my sincere thanks to Dr. B. S. Oppenheimer, Dr. H. Wessler and to Dr. L. A. Conner for their helpful suggestions. I am indebted to Miss Lydia Buechi for her kind assistance.

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STUDIES ON THE EFFECT OF NITROGLYCERIN, AMYL NITRITE AND ACETYLCHOLINE ON HYPERTENSION*

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THE medicinal treatment of hypertension is frequently unsatisfactory and the results, when obtained, are often only temporary. The resulting disappointment is due in great part to adherence to the widespread and traditional belief that nitrites and other substances reduce blood pressure regardless of the cause. Much of the clinical evidence upon which this belief is maintained is based on observations not properly controlled, and reduction in blood pressure is frequently due in great part to such factors as rest in bed, diet, and limitation of fluid intake rather than to the effect of the drugs used.

In view of the contradictory reports in the literature on this subject it was decided to study the effect of nitroglycerin, amyl nitrite, and acetylcholine (acecoline) in a selected and controlled group of cases. The acetylcholine was obtained directly from the Anglo-French Drug Company, the nitroglycerin and amyl nitrite were taken from the hospital supply.

METHOD OF STUDY

Ten patients with hypertension and renal involvement were selected for this experiment and 10 additional normal persons were used as controls. The hypertension patients were first examined physically for clinical evidences of renal disease. The average concentration of urea in the blood was 30 mg. per 100 c.c. and the average creatinine was 2.5 mg. The urine was of low specific gravity with little variation during the day or night. The night urine averaged about 900 c.c. The power of concentration, dilution, and excretion of water was impaired in all patients. The blood pressure averaged 195 mm. of mercury.

All patients were kept in bed on a low protein and salt poor diet and the total fluid intake was limited to 1500 c.c. in twenty-four hours. The blood pressure was taken twice a day by the auscultatory method, using a mercury manometer. The drugs were not given until the blood pressure was reduced to a fixed level by this management, in order to exclude the factors of rest, diet, and limitation of fluid intake. All three drugs were used on each of the patients and on the controls at suitable intervals in order to compare their effects on the same

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individual. After administration of the drugs, blood pressure readings were made every two minutes for an hour and then at frequent intervals for the next twenty-four hours.

RESULTS

Nitroglycerin, gr. $\frac{1}{50}$, was given under the tongue to 10 normal persons after the blood pressure level was previously established. The maximum effect occurred in two minutes, the average maximum drop of the systolic pressure was 18 mm., and the average reduction in the diastolic pressure was 6 mm. The systolic pressure remained low for fifteen minutes and was not followed by a rise above the former level, while the diastolic pressure remained below the original pressure for six minutes and was often then followed by a rise of from 5 to 8 mm. above the previous normal level. This reaction lasted an average of fifteen minutes. All normal persons showed a fall and subsequent rise very similar to the manner described.

Table I

Normal Controls

Effect of Nitroglycerin (Gr. $\frac{1}{50}$)

Time elapsing before maximum effect	Maximum effect	Duration	Reaction	
			Intensity	Duration
		Systolic		
2 min.	18 mm.	15 min.	None	None
		Diastolic		
2 min.	6 mm.	9 min.	6 mm.	18 min.

Table II

Normal Controls

Effect of Amyl Nitrite (2 Ampules)

Time elapsing before maximum effect	Maximum effect	Duration	Reaction	
			Intensity	Duration
		Systolic		
4 min.	46 mm.	21 min.	None	None
		Diastolic		
2 min.	38 mm.	20 min.	None	None

Nitroglycerin, gr. $\frac{1}{50}$, under the tongue was given to 10 patients with hypertension and renal disease after the precautions before mentioned were taken. No effect was observed on the systolic pressure in 3 cases and no drop of the diastolic pressure occurred in 6 instances. The maximum effect on the systolic pressure in the remainder occurred in from two to seven minutes, the maximum fall varied from 4 to 40 mm., and the original pressure returned in from two to eighteen minutes. In 6 cases the pressure rose above the original level, the rise amounting to from 4 to 20 mm. and lasting from two to thirty minutes. The

diastolic pressure dropped in only 4 of the 10 cases. The drop varied from 6 to 14 mm. and lasted from three to twenty minutes. A subsequent rise above the previous level occurred in 6 patients, varying from 8 to 24 mm. and lasting from three to thirty minutes. No subsequent changes were observed during the following twenty-four hours, either in the systolic or diastolic pressures.

Amyl nitrite was administered by inhalation of two ampules held to the nose under a handkerchief. The normal cases showed a maxi-

TABLE III

HYPERTENSION

EFFECT OF AMYLNITRITE (2 AMPULES) ON SYSTOLIC PRESSURE

CASE NO.	TIME ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION	REACTION	
				INTENSITY	DURATION
I	2 min.	56 mm.	8 min.	24 mm.	7 min.
III	3 min.	40 mm.	3 min.	6 mm.	6 min.
IV	2 min.	64 mm.	5 min.	4 mm.	3 min.
V	3 min.	88 mm.	4 min.	10 mm.	8 min.
VI	4 min.	70 mm.	6 min.	None	None
VII	1 min.	108 mm.	5 min.	10 mm.	4 min.
VIII	2 min.	70 mm.	7 min.	None	None
IX	2 min.	42 mm.	5 min.	14 mm.	12 min.
X	3 min.	66 mm.	7 min.	8 mm.	3 min.

TABLE IV

HYPERTENSION

EFFECT OF AMYLNITRITE ON DIASTOLIC PRESSURE

CASE NO.	TIME INTERVAL ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION	REACTION	
				INTENSITY	DURATION
I	2 min.	68 mm.	5 min.	8 mm.	5 min.
III	3 min.	12 mm.	3 min.	None	None
IV	2 min.	56 min.	10 min.	14 mm.	10 min.
V	3 min.	86 mm.	5 min.	16 mm.	6 min.
VI	3 min.	46 mm.	7 min.	6 mm.	8 min.
VII	1 min.	62 mm.	10 min.	None	None
VIII	2 min.	30 mm.	6 min.	None	None
IX	2 min.	28 mm.	6 min.	12 mm.	15 min.
X	3 min.	38 mm.	7 min.	None	None

mum drop of the systolic pressure in three minutes amounting to 45 mm. and returning to normal in twenty minutes. The maximum drop in diastolic pressure occurred in two minutes, amounted to 35 mm. and the pressure returned to normal in twenty minutes. No subsequent elevation of either the systolic or diastolic pressures to a level above the previous normal occurred in the control cases in contrast to those seen after nitroglycerin.

The effect of amyl nitrite on the patients with hypertension was quite marked. The maximum drop in systolic pressure occurred in from one to three minutes, amounted to from 40 to 108 mm., and returned to the previous level in from three to eight minutes. All but

2 of these patients showed a reaction rise above the previous level amounting to from 4 to 24 mm. and lasting from three to twelve minutes. The diastolic pressure fell in from one to three minutes to from 12 to 86 mm. and remained below the original diastolic pressure from three to ten minutes. A reaction rise above the previous level of the diastolic pressure occurred in all but 4 instances amounting to from 6 to 14 mm. and lasting from five to fifteen minutes. Observations during the next twenty-four hours failed to show any appreciable variation in either the systolic or diastolic pressures.

TABLE V

HYPERTENSION

EFFECT OF NITROGLYCERIN (GR. 1/50) ON SYSTOLIC PRESSURE

CASE NO.	TIME INTERVAL ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION OF EFFECT	REACTION	
				DURATION	INTENSITY
I	3 min.	12 mm.	4 min.	30 min.	20 mm.
III	7 min.	32 mm.	18 min.	None	None
IV	No effect	No effect	No effect	15 min.	10 mm.
V	5 min.	5 mm.	4 min.	2 min.	5 mm.
VI	No effect	No effect	No effect	None	None
VII	2 min.	4 mm.	2 min.	9 min.	12 mm.
VIII	3 min.	4 mm.	3 min.	12 min.	5 mm.
IX	3 min.	40 mm.	18 min.	None	None
X	No effect	No effect	No effect	10 min.	4 mm.

TABLE VI

HYPERTENSION

EFFECT OF NITROGLYCERIN (GR. 1/50) ON DIASTOLIC PRESSURE

CASE NO.	TIME ELAPSING BEFORE MAXIMUM EFFECT	MAXIMUM EFFECT	DURATION	REACTION	
				DURATION	INTENSITY
I	No effect	No effect	No effect	30 min.	24 mm.
III	No effect	No effect	No effect	None	None
IV	No effect	No effect	No effect	25 min.	16 mm.
V	3 min.	6 mm.	5 min.	None	None
VI	9 min.	8 mm.	20 min.	None	None
VII	2 min.	14 mm.	3 min.	8 min.	10 mm.
VIII	No effect	No effect	No effect	3 min.	8 mm.
IX	No effect	No effect	No effect	6 min.	18 mm.
X	No effect	No effect	No effect	8 min.	12 mm.

Acetylcholine (acecoline) was given in doses of 0.2 gm. subcutaneously but appreciable changes could not be determined in the systolic or diastolic pressures either in the normal or hypertensive subjects. The readings were taken every two minutes for an hour and at short intervals for the next twenty-four hours, but no fall in pressure was observed. This is in marked contrast to the reports of M. Villaret and L. Justin-Besançon[1, 2] who state that the pressure is reduced because of a vasodilator action on the arteries and arterioles. The same authors claim a remarkable effect in arteritis and in senile and diabetic gangrene. The effect of this drug was studied on the central

artery of the retina in normal persons by these authors in collaboration with Schiff-Wertheim[3] and dilatation was observed ophthalmoscopically in 11 of 25 persons examined. It is also stated that no local or general reactions occurred. All of our patients, however, complained of local pain after the injection.

A comparison of the effects of the substances used on the same patient showed that the change after nitroglycerin in our cases of hypertension was inconstant, while amyl nitrite caused a marked fall in every instance. The reduction after amyl nitrite was much greater than after nitroglycerin and the effect lasted almost as long. It is interesting to note that the pressure did not rise to a higher level than originally after amyl nitrite in the control cases, while nitroglycerin often did show such a rise. No change in the blood pressure was noted after acetylcholine, although amyl nitrite and nitroglycerin caused definite reduction in the same patients.

SUMMARY

1. A series of patients with hypertension and renal involvement were given nitroglycerin, amyl nitrite, and acetylcholine after the blood pressure was previously reduced to a fixed level by bed rest, diet, and limitation of fluid intake. The results were controlled by a study of a similar series of normal persons.

2. Nitroglycerin, gr. $\frac{1}{150}$, under the tongue produced a fall in blood pressure in all the normal controls, but this effect was inconstant in the patients with hypertension.

3. Amyl nitrite caused a fall in pressure in the controls and hypertensive cases in every instance, being effective also in those instances where nitroglycerin failed to act.

4. A reaction in the form of a temporary rise to a level above that existing before the administration of the drug occurred in a large proportion of the cases with hypertension receiving amyl nitrite or nitroglycerin. The control cases receiving nitroglycerin showed a similar reaction rise, but not those after amyl nitrite. This rise may be of some clinical value in cases of impending or actual cerebral hemorrhage.

5. The effect of amyl nitrite in the doses used was much more marked and lasted almost as long as after nitroglycerin but headache, vertigo, and flushing were more marked after the former drug.

6. Acetylcholine was found to be inert in both the controls and the cases of hypertension, in contradistinction to the claims made in the literature.

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STUDIES ON THE CIRCULATION

II. Cardiac Output in Diseases of the Heart, and Under the Influence of Digitalis Therapy*

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THE circulation of normal human beings can increase in magnitude in response to the greater demands which effort puts upon it. It may increase from three to four times the resting value, and in exceptional cases, as in athletes driven to exhaustion, still more.[1] Analysis of the source of this immense reserve power has led to the conception of the reserve factors in functional sufficiency of the circulation.

Two of these lie in the heart itself, the ventricular output (stroke volume) and ventricular rate. The increase in the rate is the most familiar response to effort and the only one clinically recorded. Its maximal efficient limit is probably not more than twice the resting level. Beyond this increase the efficiency of the heart undoubtedly suffers, because the diastolic interval becomes too short for adequate filling of the heart and for rest for the ventricles.

The ventricular output or stroke volume is clinically rarely estimated and until recently has not been measured at all. Late investigations[2] have shown the magnitude of this factor to depend upon the weight of the subject. It is now well established that the stroke volume divided by the kilograms of body weight is a comparative constant (stroke index) of the average order of 1.5 c.c. That is to say a normal 70 kg. man would have a stroke volume or an output of the heart per beat of about 100 c.c. (70 X 1.5). This stroke index is a useful basis of comparison between the normal and abnormal.

To what extent the stroke volume responds to increased effort has long been debated. It is now clear that in fit and trained subjects it may increase perhaps twofold under severe effort.[3] Under ordinary circumstances in people out of condition this powerful reserve is called on to a lesser degree.

These two factors, stroke volume and ventricular rate, increasing together can under optimal conditions account for a fourfold rise in the minute volume of blood flow (ventricular rate × stroke volume), which is the response of the circulation to the greatest demand that effort puts upon it.

Two other reserve factors, less familiar, are entirely independent of the heart, residing in the blood and muscles of which they are re-

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markable properties. It is necessary to recall the respiratory function of the circulation to make their rôle clear. A greater circulation is needed in exercise in order to remove the increasing quantities of carbon dioxide and to bring fresh supplies of oxygen to restore the lactic acid, produced by muscular contraction, to its precursor. If the circulation for the moment is considered as a means of transporting oxygen from lungs to tissues, it will become clear that since under resting conditions arterial blood gives up only about 25 per cent of its oxygen, a great reserve resides in the possibility of its giving up, let us say, 50 per cent of its oxygen content. In other words the circulation may become twice as effective in its primary function by this means. The difference between the oxygen content of arterial and venous blood will indicate the extent to which this reserve factor is being utilized. It is more convenient to refer to this factor in direct values rather than in percentage. Thus, since the average oxygen content of 100 c.c. of arterial blood is about 20 c.c. and of venous blood about 16 c.c., the difference normally is 4 c.c. An arteriovenous oxygen difference of more than 4 c.c. will, therefore, have the same significance as a rise in pulse rate or stroke volume, that is, to indicate that one of the reserves of the circulation is being called upon. It has been observed that on normal human beings who are not in condition or under special training,[3] the arteriovenous oxygen difference and the ventricular rate are the first reserves of the circulation drawn on under increased effort. Although it is a primary factor in an effective circulation, the arterial oxygen utilization is rarely estimated clinically.

The fourth reserve does not concern us especially, because it is not measurable by the method which we have employed in studying the other reserves. It relates to the ability of muscles to work under an oxygen deficit which the circulation erases after the effort has subsided.

Before we can proceed to the quantitative consideration of these factors in diseases of the heart and vascular system, it is necessary to know the extent to which the circulation is using its reserves under normal conditions. In an earlier publication[4] we gave our experience with the Henderson and Haggard, ethyl iodide method for measuring the circulation in normal human beings. We presented also the data we collected by this means on normal male and female subjects at rest. For the purposes of our present investigation we may adopt the resting values found in this study as normal standards under the conditions and with the method with which we have worked. Our general findings are summarized in Table I.

That is to say, at rest normal human beings receive on the average a discharge of blood to each kilogram of body weight per beat of the heart (stroke index) of 1.5 c.c. Since the total weight determines the total output per beat of the ventricles, a 70 kg. man will have a stroke

TABLE I

DATA ON THE CIRCULATION OF NORMAL SUBJECTS

OBSERVATIONS	WT. KILOGRAMS	ALVEOLAR CO_2 PER CENT	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT— PER KILOGRAM	ARTERIOVENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD
32 Males	68	5.6	8.1	78	102	1.5	3.5
27 Females	58	5.4	7.3	79	93	1.6	3.3

volume therefore of about 100 c.c. By calling on a ventricular rate of from 70 to 80 beats per minute, the circulation achieves a resting minute volume of between 7 and 8 liters. With this volume of blood flow, the tissues need utilize only from 3 to 4 c.c. of oxygen of every 100 c.c. of blood, to cover resting metabolic requirements.

From the clinical standpoint it would be desirable to know how these quantitative factors of the circulation function in heart disease as compared with the normal. Does the range of the reserves become limited? How is the task of maintaining an adequate circulation distributed among them? Is there a difference between mechanical valvular abnormalities and myocardial degeneration? What are the effects of disturbances of rhythm? What happens in heart failure? What is the effect of digitalis therapy?

As a step toward supplying data for an accurate answer to some of these questions, we offer in the present study 340 measurements of the factors of the circulation on 63 patients suffering from a variety of diseases of the cardiovascular system. Resting subjects only were employed, for the obvious reason that most of the cases studied showed far-advanced lesions. About half the cases were in circulatory sufficiency at rest. The others showed clinical symptoms and signs of cardiac insufficiency at rest. The cases have been arranged in ten definitely defined anatomical and etiological groups.

EXPERIMENTAL DATA

1. *Influence of the Pulmonary Factor.*—In measuring the circulation by any method, especially the ethyl iodide method, we really measure the volume flow of blood from right to left heart through the lungs. The accuracy of this method is dependent upon a free exchange of respiratory gases between the alveoli and the pulmonary capillaries. It will be seen that the cases studied presented for the most part advanced lesions. In view of the frequent, inevitable occurrence of congestion of the lungs, sometimes so slight as only to be inferred from symptoms, at other times sufficiently marked to be detected by physical and x-ray signs, it is reasonable to inquire how such a condition or the presence of a hydrothorax affects the value of the data derived. This is not an easy point to investigate with decision on cardiac cases which present other variable factors. It is necessary to use cases with affections of the lungs uncomplicated by heart disease, in which congestive, exudative and sclerotic lesions of different degrees exist. Accordingly we selected a variety of cases of pulmonary tuberculosis in order to test this point.* The findings are recorded in Table II.

It will be seen that the blood flow was constant on the average, irrespective of how much lung was involved. The average minute vol-

*We are greatly indebted to Dr. J. J. Wiener of the division of tuberculosis of the hospital for selecting these cases. Detailed report of this phase of the work will be published elsewhere.

ume was 6.2 liters, and the average weight of these patients was 51 kilograms. Table XIV, in which all our cases are compared on the basis of equal weights, will disclose that these figures compare almost exactly with our normal cases. The lower stroke index (1.2) was due entirely to the more rapid average ventricular rate of the tubercular patients. Moreover, it will be noted that the arteriovenous oxygen difference was also within normal limits. This fact, as we shall later see, is of great significance in demonstrating a circulation that is in normal relation to the metabolism of the subject.

2. *Rheumatic Mitral Stenosis, Regular Rhythm.*—The data on the 6 cases of this group are contained in Table III. So far as we could clinically determine only the mitral valve was involved, but the lesion in each case was anatomically advanced. Cases 1 and 4 were fully compensated, and it is interesting to note that all the factors of the circulation were normal by an ample margin. Cases 2 and 6 had definite symptoms and signs of cardiac insufficiency although not advanced, inasmuch as the patients were capable of leaving their beds on and off. The latter patient improved under rest to a point where the liver receded and moderate activity was resumed. In both cases the stroke index was fixed at the lowest level of normal. That the minute volume was not quite adequate for resting requirements was indicated by the definite increase in the arteriovenous oxygen difference, which is to say that at rest the body was drawing to a considerable extent on a reserve of the circulation ordinarily used only in effort. Patients in Cases 3 and 5 were bedridden with advanced cardiac insufficiency. The factors of the circulation showed a wide quantitative departure from normal standards. There was a marked rise in the ventricular rate, a striking fall in the stroke volume and index and a great increase in the arteriovenous oxygen difference. These findings were typical of clinical cardiac insufficiency, from whatever cause, as we shall presently see.

3. *Rheumatic Mitral Stenosis, Auricular Fibrillation.* 4. *Rheumatic Combined Mitral Stenosis and Aortic Insufficiency, Mitral Stenosis Predominating, Auricular Fibrillation.*—These two groups although clinically separable may, from a functional standpoint, be treated together. The data of the 10 cases are recorded in Tables IV and V. Cardiac insufficiency of varying degrees and chronicity and auricular fibrillation were features of all the cases. They all received digitalis therapeutically or experimentally.

On Cases 10, 11, 12, 13, and 14 there were blood flow determinations before digitalis treatment was begun and during periods when the digitalis was discontinued. It will be noted at once that departures from normal in all the factors of the circulation that characterized cardiac insufficiency in the cases of mitral stenosis with a regular rhythm (Group II) were duplicated in this group. The ventricular

TABLE II

CIRCULATION IN ADVANCED TUBERCULOSIS OF THE LUNGS

NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
A.E.	4.8	299	7.9	119	66	1.2	3.8	Unilateral hydrothorax.
	4.7	307	7.5	122	61	1.1	4.3	
D.L.	5.6	277	5.5	66	83	1.5	5.0	Unilateral pyopneumothorax.
	5.7	223	5.4	70	78	1.4	4.1	
A.H.	4.4	189	5.2	113	46	1.1	3.6	Unilateral pyopneumothorax.
	5.0	187	4.5	105	43	1.0	4.2	
P.N.	5.5	216	7.4	99	75	1.4	2.9	Unilateral hydropneumothorax.
	5.6	198	5.6	91	62	1.1	3.5	
	5.2		6.1	98	64	1.2	3.9	Averages
D.F.	5.5	219	7.4	120	62	1.3	3.0	Advanced tuberculosis of right side. Fibrosis and cavitation. Heart pulled to right.
	5.6	208	4.7	108	44	0.9	4.5	
S.W.	5.8	324	11.0	95	116	2.2	2.9	Extensive tuberculosis of right side.
	5.4	292	7.6	91	84	1.6	3.9	Left lung practically negative.
M.K.	5.3	267	8.0	108	74	1.2	3.3	Predominant infiltration of right side with thickened pleura.
	5.4	265	8.1	105	77	1.3	3.3	
B.G.	4.6	185	6.0	105	57	1.0	3.0	Advanced tuberculosis with fibrosis of right side. Thickened pleura.
	4.8	198	5.0	104	48	0.9	4.0	
S.B.	3.8	217	7.0	122	57	1.2	3.1	Chronic fibrophthisis and cavitation mainly on right side. Bronchiectasis.
	4.6	231	5.9	109	54	1.1	4.0	
E.W.	4.7	197	5.5	119	46	0.9	4.0	Chronic tuberculosis of right side with cavitation. Left slight.
	4.4	208	5.1	126	40	0.7	4.1	
S.G.	4.7	207	5.4	128	42	1.0	3.9	Dense thickened pleura and cavitation on left side. Right negative.
	4.7	214	4.6	121	38	0.9	4.6	
	5.0		6.2	111	60	1.2	3.7	Averages

TABLE II—CONT'D

NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
E.B.	5.4	295	6.6	97	68	0.9	4.5	Bilateral advanced fibroid tuberculosis with emphysema and bronchitis.
	5.7	213	6.6	98	68	0.9	3.2	
B.K.	4.0	274	5.6	104	54	1.2	4.9	Bilateral extensive tuberculosis of all lobes with cavitation.
	3.4	262	5.8	94	62	1.4	4.5	
I.K.	4.4	289	6.2	85	73	1.4	4.7	Bilateral extensive fibrocaseous tuberculosis.
	4.6	237	5.0	79	63	1.2	4.8	
M.L.	4.4	279	7.5	65	114	1.3	3.7	Bilateral extensive tuberculosis. Diffuse nodular infiltrations.
	4.6		8.0	66	120	1.4		
I.N.	5.4	235	5.1	92	57	1.0	4.7	Bilateral fibrocaseous tuberculosis of upper lobes. Cavitation and fibrosis.
	5.4	266	5.3	89	59	1.1	5.0	
A.H.	4.2	221	7.9	109	73	1.1	2.8	Bilateral advanced tuberculosis.
	4.2	334	9.4	104	90	1.4	3.6	
J.D.	4.5	180	9.4	126	75	1.4	1.9	Bilateral extensive tuberculosis.
	3.7	266	8.6	119	72	1.4	3.1	
I.K.	5.4	252	4.2	70	60	1.1	6.0	Bilateral fibrocaseous tuberculosis of upper lobes with emphysema and bronchitis.
	5.4	252	4.1	71	57	1.1	6.2	
D.Y.	4.5	202	4.9	59	83	1.4	4.1	Bilateral fibrocaseous tuberculosis of upper lobes with emphysema and bronchitis.
	4.4	180	4.6	59	78	1.4	3.9	
A.G.	4.8	206	6.0	88	68	1.3	3.4	Bilateral diffuse chronic nodular miliary tuberculosis.
	5.1	217	5.0	80	63	1.2	4.3	
	4.6		6.3	90	73	1.2	4.2	Averages

TABLE III

PURE MITRAL STENOSIS; REGULAR RHYTHM

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
6/ 5/28	Case 1	5.1	206	6.9	95	73	2.3	3.0	No digitalis.
	A.W.	5.1	192	6.6	93	71	2.2	2.9	
3/22/28	Case 2	3.4	302	6.0	73	82	1.0	5.0	No digitalis.
	S.K.	3.7	323	6.5	71	91	1.1	5.0	Alveolar CO_2 (Haldane) 3.8%.
5/ 3/28	Case 3	3.8	313	4.6	124	37	0.76	6.8	No digitalis.
	H.A.	3.8	320	3.8	126	31	0.62	8.4	
5/ 5/28		3.8	270	3.8	121	30	0.62	7.4	Alveolar CO_2 (Haldane) 4.0%.
		4.2	266	4.0	122	33	0.66	6.7	
11/ 3/27	Case 4	5.5	176	5.3	104	51	1.8	3.3	Preliminary period.
	M.K.	5.4	129	5.1	101	50	1.7	2.7	
11/10/27		5.6	124	5.3	94	56	1.9	2.4	
		5.7	129	5.4	97	56	1.9	2.3	
				5.3	99	53	1.8	2.7	Averages
12/ 8/27		5.8	205	4.7	97	49	1.7	4.4	Received 6 c.c. tincture digitalis 2 days before in 2 doses.
		5.8	205	4.4	98	44	1.5	4.7	
12/ 9/27		5.6	150	3.4	79	43	1.5	4.4	
		5.4	156	3.7	77	48	1.6	4.3	
				4.0	93	46	1.6	4.4	Averages
1/ 3/28		5.5	135	3.7	90	41	1.4	4.0	Received 18 c.c. tincture digitalis 24 hours before in 4 doses.
		5.5	172	4.0	88	45	1.6	4.3	
1/ 6/28		5.8	140	3.6	73	49	1.7	3.9	
		5.7	134	3.4	79	43	1.5	4.0	
				3.6	83	45	1.5	4.0	Averages
2/ 8/28		5.4	175	3.5	94	37	1.3	5.0	Off digitalis.
		5.5	172	3.9	96	42	1.4	4.4	
2/10/28		5.6	192	3.9	83	47	1.6	4.9	
		5.6	182	3.8	80	41	1.4	5.0	
				3.8	90	42	1.4	4.8	Averages

TABLE III—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
2/20/28		5.6	171	4.2	75	56	1.9	4.1	Off digitalis.
		5.5	169	4.3	78	55	1.9	4.0	
2/24/28		5.6	148	4.3	86	50	1.7	3.5	
		5.5	147	4.6	91	51	1.8	3.2	
				4.4	88	53	1.8	3.7	Averages
12/20/27	Case 5 E.S.	3.7	190	2.8	136	20	0.75	7.0	Preliminary period.
		3.7	179	2.4	135	18	0.65	7.5	Alveolar CO_2 (Haldane) 4.0%.
12/22/27		3.6	149	2.2	139	17	0.63	9.1	
		3.6	223	2.5	134	19	0.70	8.8	
				2.5	136	19	0.68	8.1	Averages
1/12/28		3.9	192	2.5	134	19	0.69	7.7	Received 9 c.c. tincture digitalis
1/13/28		4.0	206	2.3	121	19	0.69	7.2	2 days before in 3 doses.
		4.0	161	2.7	118	20	0.83	7.6	
				2.5	120	20	0.74	7.6	Averages
2/11/28		3.3		2.4	135	18	0.66		Off digitalis.
		3.3	124	1.9	130	15	0.53	6.6	
2/15/28		3.5	162	2.0	127	16	0.60	7.8	
		3.6	170	1.8	130	14	0.50	9.8	
				2.0	131	16	0.58	8.0	Averages
3/22/28	Case 6 M.K.	4.3	242	3.5	73	48	1.1	6.8	Preliminary period.
		4.2	223	4.1	76	54	1.2	5.5	Alveolar CO_2 (Haldane) 4.1%.
3/29/28		4.1	217	4.3	74	57	1.3	5.1	
		4.2	233	4.1	72	57	1.3	5.7	
				4.0	74	54	1.2	5.8	Averages
4/10/28		4.5	245	3.9	69	57	1.3	6.3	Received 12 c.c. tincture dig-
		4.6	230	4.1	69	60	1.3	5.8	italis 2 days before.
4/11/28		4.3	270	3.9	78	51	1.1	6.8	
		4.3	271	4.2	77	55	1.2	6.4	
				4.0	73	56	1.2	6.3	Averages

TABLE IV

PURE MITRAL STENOSIS; AURICULAR FIBRILLATION

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	APEX RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
10/14/27	Case 7 A.E.	3.2	242	3.9	91	42	0.92	6.3	Partially digitalized
4/17/28	Case 8 L.N.	5.0	263	6.0	62	92	1.1	4.4	Fully digitalized
		5.0	258	5.3	65	85	1.0	5.0	
7/20/28	Case 9 M.S.	3.9	290	5.9	91	65	1.1	4.9	p. d.* 9 Partially digitalized
		4.3	214	5.4	88	62	1.1	4.0	p. d. 7
7/21/28		4.1	238	5.7	82	70	1.2	4.2	p. d. 6
		4.4	215	6.2	82	75	1.3	4.0	p. d. 8
12/ 9/27	Case 10 I.J.	4.0	241	4.1	119	34	0.68	6.0	p. d. 15 Preliminary period
12/10/27		3.8	274	3.9	126	31	0.61	7.0	p. d. 14
		4.2	233	3.8	114	34	0.67	6.1	p. d. 14
				3.9	120	33	0.65	6.3	Averages
12/11/27		4.3	239	4.0	100	40	0.79	6.0	p. d. 6 Received 3 c.c. tincture
12/12/27		4.3	218	3.9	89	44	0.89	5.6	p. d. ? digitalis and 2. 5 c.c.
12/14/27		4.1	234	3.7	114	32	0.65	6.4	p. d. ? every day thereafter
12/16/27		4.2	200	3.6	91	39	0.71	5.6	p. d. ?
		4.2	181	3.2	87	36	0.66	5.8	p. d. ?
				3.7	96	38	0.74	5.9	Averages
11/ 3/27	Case 11 J.W.	4.7	211	3.9	117	33	0.98	5.5	p. d. 14 Preliminary period
		4.7	195	4.0	108	37	1.1	4.9	p. d. 14 Alveolar CO_2 (Haldane)
11/ 8/27		4.3	234	3.3	100	33	0.96	7.2	p. d. 12 4.9%
		4.3	190	3.7	104	36	1.1	5.1	p. d. 13
				3.7	107	35	1.03	5.7	Averages
11/16/27		4.6	189	3.7	91	41	1.2	5.1	p. d. 7 Received 7 c.c. tincture
		4.6	184	4.0	94	43	1.3	4.6	p. d. 5 digitalis and 2 c.c. daily
11/18/27		4.9	189	4.3	91	42	1.2	4.4	p. d. 4 for next 18 days
		4.8	190	3.8	90	42	1.2	5.1	p. d. 0
11/25/27		4.9	158	4.3	73	60	1.7	3.7	p. d. 0
		4.9	179	4.2	67	63	1.8	4.4	p. d. 0
12/ 3/27		5.0	174	4.3	65	67	2.0	4.0	p. d. 0

TABLE IV—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	APEX RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS	
		4.9	184	4.0	65	62	1.8	4.6	p. d. 0	
2/22/28		4.4	206	3.1	100	31	0.91	6.9	p. d. 14	Digitalis discontinued 35
		4.3	216	3.1	94	32	0.95	7.2	p. d. 13	days preceding
2/23/28		4.5	199	3.3	99	33	0.96	6.2	p. d. 13	
				3.2	98	32	0.94	6.8	Averages	
11/17/27	Case 12	4.8	238	4.6	113	41	1.1	5.2	p. d. 14	Preliminary period
11/21/27	F.M.	5.0	228	4.2	114	37	1.0	5.4	p. d. 13	
		5.0	235	4.8	109	44	1.2	4.9	p. d. 13	
				4.5	112	41	1.1	5.2	Averages	
11/25/27		5.0	225	5.2	101	51	1.4	4.4	p. d. 7	Received 7 c.c. tincture
		5.0	220	5.0	102	49	1.3	4.4	p. d. 5	digitalis day before
11/28/27		4.9	209	4.5	75	47	1.3	4.7	p. d. 4	
		5.1	219	4.5	100	45	1.2	4.8	p. d. 4	
12/ 1/27		5.0	209	4.1	90	46	1.2	5.1	p. d. 4	
		5.1	212	4.7	91	52	1.4	4.5	p. d. 4	
				4.7	97	48	1.3	4.7	Averages	
2/21/28		4.8	227	4.3	114	38	1.0	5.3	p. d. 17	Digitalis discontinued 23
		5.0	240	4.8	119	40	1.1	5.1	p. d. 15	days preceding
2/22/28		4.8	211	4.8	113	42	1.1	4.4	p. d. 12	
				4.6	115	40	1.1	4.9	Averages	
3/ 5/28		5.2	224	4.6	89	52	1.4	4.8	p. d. 0	Received 12 c.c. tincture
		5.1	227	4.5	88	50	1.4	5.1	p. d. 0	digitalis day before
3/ 6/28		5.0	198	4.1	78	52	1.4	4.9	p. d. 0	
				4.3	85	51	1.4	4.9	Averages	
6/21/28		5.1	203	4.9	64	76	2.1	4.2	p. d. 0	Received 2 to 3 c.c. tinc-
		5.1	210	4.9	65	75	2.0	4.3	p. d. 0	ture digitalis daily for
6/26/28		5.0	181	4.4	69	64	1.7	4.2	p. d. 0	preceding 3 months
		5.0	204	5.0	69	72	1.9	4.1	p. d. 0	
				4.8	67	72	1.9	4.2	Averages	

*Note.—p. d. = pulse deficit.

TABLE V

COMBINED MITRAL STENOSIS AND AORTIC INSUFFICIENCY, MITRAL STENOSIS PREDOMINATING, AURICULAR FIBRILLATION

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	APEX RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
11/ 4/27	Case 13	3.9	171	3.6	133	27	0.76	4.8	p. d. 11 Preliminary period
11/ 8/27	C. H.	4.0	168	3.6	135	27	0.75	4.8	p. d. 10 Alveolar CO_2 (Haldane)
		3.9	155	3.5	123	29	0.80	4.4	p.d. 10 4.4%
				3.6	130	28	0.77	4.7	Averages
11/16/27		4.4	173	3.3	84	39	1.1	5.2	p. d. 3 Received 12 c.c. tincture
11/17/27		4.6	170	3.6	83	43	1.2	4.7	p. d. 4 digitalis 4 days before
		4.7	170	3.3	85	39	1.1	5.0	p. d. 4 and 1 c.c. daily there-
11/23/27		5.2	201	4.1	104	39	1.1	4.9	p. d. 10 after
		5.0	192	4.0	92	43	1.2	4.8	p. d. 10
				3.7	89	41	1.1	4.9	Averages
1/30/28		4.5	199	3.6	122	29	0.82	5.6	p. d. 9 Digitalis discontinued 13
		4.6	210	3.7	116	32	0.88	5.7	p. d. 9 days preceding
2/ 1/28		4.9	237	3.1	125	25	0.69	7.3	p. d. 10
		4.7	232	3.7	128	29	0.81	6.3	p. d. 10
				3.5	123	29	0.80	6.2	Averages
2/16/28		4.8	170	3.1	79	39	1.1	5.6	p. d. 3 Received 12.5 c.c. tincture
		4.9	163	3.4	79	42	1.2	4.6	p. d. 3 digitalis 5 days before
2/18/28		4.6	206	4.2	88	47	1.3	5.0	p. d. 4 and 1.5 c.c. daily there-
		5.1	202	3.8	90	42	1.2	5.4	p. d. 4 after
				3.6	84	43	1.2	5.2	Averages
6/23/28		4.8	179	4.1	65	63	1.6	4.4	p. d. 0 Received 2 c.c. tincture
		4.9	163	3.6	64	57	1.4	4.5	p. d. 0 digitalis daily for pre-
6/28/28		4.7	173	4.3	70	62	1.5	4.0	p. d. 0 ceding 3 months
		4.8	171	3.9	69	57	1.4	4.4	p. d. 0
				4.0	67	60	1.5	4.3	Averages

TABLE V—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS	
5/ 4/28	Case 14 S. G.	5.6	204	3.8	96	40	0.81	5.4	p. d. 4	Preliminary period
		5.3	200	4.1	94	43	0.89	4.9	p. d. 4	
				4.0	95	42	0.85	5.2	Averages	
5/ 8/28		5.3	185	4.0	82	48	0.98	4.7	p. d. 0	Received 6 c.c. tincture digitalis 2 days before and 2 c.c. daily thereafter
		5.4	183	3.8	80	46	0.96	4.9	p. d. 0	
				3.9	81	47	0.97	4.8	Averages	
6/20/28		5.5	196	5.0	72	70	1.4	3.9	p. d. 0	Received 2 c.c. tincture digitalis daily for preceding 6 weeks
		5.1	191	4.6	72	63	1.3	4.2	p. d. 0	
7/14/28		5.4	231	5.5	92	60	1.2	4.2	p. d. 0	
		5.3	237	5.0	81	62	1.3	4.8	p. d. 0	
				5.0	79	64	1.3	4.3	Averages	
6/12/28	Case 15 R. S.	4.1	210	2.8	84	33	0.74	7.6	p. d. 4	Received 2 c.c. tincture digitalis daily for 2 months preceding
6/14/28		4.4	204	3.2	60	53	1.2	6.5	p. d. 0	
		4.3	208	2.7	68	40	0.90	7.6	p. d. 0	
8/17/28	Case 16 C. D.	3.9	282	4.4	80	55	1.1	6.5	p. d. 0	Fully digitalized
		3.8	281	5.1	82	62	1.3	5.6	p. d. 0	
8/18/28		3.8	285	4.4	83	53	1.1	6.5	p. d. 0	
		3.6	282	4.4	83	53	1.1	6.5	p. d. 0	
9/14/28		3.5	242	4.2	80	52	1.1	5.8	p. d. 0	
		3.4	279	3.7	73	51	1.1	7.5	p. d. 0	

TABLE VI

PURE AORTIC INSUFFICIENCY; REGULAR RHYTHM

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4/17/28	Case 17 M. D.	5.8	254	6.3	75	84	1.6	4.0	No digitalis
		6.0	252	6.2	71	88	1.7	4.1	
4/13/28	Case 18 A. J.	4.6	346	8.8	78	114	1.8	4.0	No digitalis
		4.0	448	8.8	82	107	1.7	5.1	
12/20/27	Case 19 S. W.	5.6	184	5.0	118	42	1.4	3.7	Preliminary period
		5.7	150	5.6	118	48	1.5	2.7	
		5.6	183	5.5	109	50	1.6	3.4	
12/22/27		5.4	174	6.0	109	55	1.8	2.9	
				5.5	113	49	1.6	3.2	Averages
1/12/28		5.7	182	5.5	114	48	1.6	3.3	Received 11 c.c. tincture digitalis 2 days before
		5.6	193	5.7	112	51	1.6	3.3	
1/13/28		6.0	180	5.5	110	50	1.6	3.4	
				5.6	112	50	1.6	3.3	Averages
2/14/28		5.3	186	4.3	112	38	1.2	4.4	Digitalis discontinued preceding 38 days
		5.2	203	4.9	110	45	1.5	4.1	
2/15/28		5.5	195	4.3	108	39	1.3	4.6	
		5.4	191	5.0	106	47	1.5	3.8	
				4.6	109	42	1.4	4.2	Averages
11/ 2/27	Case 20 J. S.	5.0	248	5.0	96	52	1.3	5.0	Preliminary period
			242	5.5	94	58	1.5	4.4	
11/10/27		4.8	198	5.4	93	58	1.5	3.9	
				5.3	94	56	1.4	4.4	Averages
12/19/27		5.1	213	4.4	80	55	1.4	4.8	Received 14 c.c. tincture digitalis 4 days before
		5.4	233	5.2	86	64	1.6	4.2	
12/21/27		4.9	243	4.5	83	55	1.4	5.3	
		4.8	245	5.2	78	66	1.7	4.8	
				4.8	82	60	1.5	4.8	Averages
1/16/28		4.9	227	5.8	86	68	1.7	3.9	Digitalis discontinued preceding 33 days
		4.8	215	5.2	87	60	1.5	4.1	
1/17/28		4.8	208	4.8	84	57	1.4	4.4	
		5.0	237	5.5	87	63	1.6	4.4	
				5.3	85	62	1.6	4.2	Averages

TABLE VI—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
11/ 1/27	Case 21 H. H.	5.0	259	8.5	96	88	1.8	3.1	Preliminary period
		5.0	311	7.6	95	80	1.6	4.1	
11/ 4/27		5.0	323	8.0	96	84	1.7	4.0	
		5.1	289	8.6	92	93	1.9	3.4	
				8.2	95	86	1.8	3.6	Averages
12/ 8/27		5.1	279	6.7	96	70	1.4	4.1	Received 17 c.c. tincture digitalis 2 days before
		5.0	282	6.3	94	67	1.4	4.5	
12/12/27		5.0	317	8.3	111	75	1.5	3.8	
		5.0	254	8.3	111	75	1.5	3.0	
				7.4	103	72	1.5	3.9	Averages
1/ 4/28		4.8	321	6.3	92	69	1.4	5.1	Digitalis discontinued 25 days preceding
		4.8	287	6.6	90	73	1.5	4.4	
1/ 5/28		4.7	254	6.0	88	68	1.4	4.2	
		4.8	297	6.2	91	68	1.4	4.8	
				6.3	90	70	1.4	4.6	Averages
12/ 5/27	Case 22 I. S.	5.6	225	6.2	69	90	2.4	3.7	Preliminary period
		5.5	212	4.9	65	75	2.0	4.4	
12/ 6/27		5.4	224	5.3	62	86	2.3	4.2	
		5.3	180	5.8	61	96	2.5	3.1	
				5.6	64	87	2.3	3.9	Averages
12/16/27		5.5	200	5.4	54	100	2.6	3.7	Received 14 c.c. tincture digitalis 2 days before
12/21/27		5.4	196	5.2	61	86	2.3	3.8	
		5.4	167	5.7	60	95	2.5	2.8	
				5.4	58	93	2.4	3.4	Averages
1/ 4/28		5.7	193	4.7	62	76	2.0	4.1	Digitalis discontinued 21 days preceding
		5.5	202	5.4	60	90	2.4	3.8	
1/ 6/28		5.3	189	5.2	63	82	2.2	3.6	
		5.5	230	4.8	62	78	2.1	4.8	
				5.0	62	81	2.2	4.1	Averages

rates were high, the stroke volumes small. The stroke indices were below 1, and the arteriovenous oxygen differences were above 5. How very markedly abnormal these constant findings were, may be more forcefully gathered from a comparison with the improved findings in those cases which had responded to effective digitalis therapy. The latter values we may assume to have been nearly the normal for these cases (11, 12, 13 and 14).

The other cases (7, 8, 9, 15, 16) were partly or completely under the influence of digitalis when the circulation was originally measured. In spite of the treatment which produced moderate clinical improvement, there were frankly normal findings in none. This is in agreement with the changes in the reserve factors of the circulation that characterize cardiac insufficiency.

In calculating the stroke volume from which the stroke index was derived, we divided the ventricular or apex rate into the minute volume of blood flow. The question arises whether in cases of auricular fibrillation, the apical rate is a measure of the number of effective ventricular strokes. In view of the fact that there is usually a pulse deficit it may be assumed that some of the cardiac contractions do not open the semilunar valves and hence cannot be regarded as producing a ventricular discharge at all. The corrected calculation on the basis of a lower effective ventricular rate (by as much as the pulse deficit) would yield higher and nearer normal values for the stroke volume and index. This point which is of considerable importance, especially in the interpretation of the influence of digitalis therapy, we shall return to later. In the present connection it may be disregarded as immaterial, since in recalculating the stroke volumes on the basis of the radial pulse rates the change in results was less than 9 per cent, still leaving the stroke volumes far from normal.

5. *Rheumatic Aortic Insufficiency, Regular Rhythm.* 6. *Rheumatic Combined Aortic Insufficiency and Mitral Stenosis, Aortic Insufficiency Predominating.*—In Tables VI and VII are recorded the blood flow determinations of these two groups. They were composed of eleven cases, nine of which gave no clinical evidence of cardiac insufficiency. It will be seen that the quantitative factors of the circulation with the exception of the pulse rate were normal or better. In spite of the advanced lesions and the obvious mechanical difficulties under which the heart was laboring, a normal circulation was maintained, adequate for resting requirements. It is interesting to note in this connection that in spite of the left ventricular enlargement, which was a feature of practically all the cases, there was no well-defined increase in the stroke volume.

The blood flow in Case 24 was definitely below normal (low stroke index and elevated arteriovenous oxygen difference). The patient had been decompensated some years before and was moderately insufficient

TABLE VII

COMBINED AORTIC INSUFFICIENCY AND MITRAL STENOSIS AORTIC INSUFFICIENCY PREDOMINATING; REGULAR RHYTHM

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
6/ 5/28	Case 23	5.6	227	6.4	92	69	1.5	3.7	No digitalis
	P. G.	5.4	217	5.9	86	69	1.5	3.7	
6/27/28	Case 24	5.2	244	4.7	91	52	1.2	5.1	No digitalis
	Y. L.	5.3	226	4.0	90	44	1.0	5.7	
7/12/28		5.2	200	5.1	102	50	1.2	3.9	
		4.9	221	4.7	102	46	1.1	4.7	
7/19/28	Case 25	5.6	250	6.3	86	74	1.6	4.0	No digitalis
	D. K.	5.4	247	6.1	93	66	1.5	4.0	
7/20/28		5.3	270	6.2	86	72	1.5	4.4	
		5.4	277	5.9	90	66	1.5	4.7	
8/14/28	Case 26	5.1	212	7.0	95	74	1.5	3.0	No digitalis
	H. H.	5.0	235	6.8	84	81	1.7	3.4	
8/16/28		4.9	225	5.8	84	69	1.4	3.9	
		4.9	203	6.1	82	74	1.5	3.4	
8/27/28	Case 27	5.0	344	8.8	69	128	1.6	3.9	No digitalis
	J. P.	5.4	314	8.0	65	124	1.6	3.9	

at the time of the investigation. In Case 26 the patient although able to get about, on and off showed unmistakable evidence of chronic decompensation. His blood flow findings were entirely normal, however. This is one of the two cases in our whole series in which the clinical and laboratory findings are in disagreement.

7. *Rheumatic Combined Aortic Insufficiency and Mitral Stenosis, No Predominance of Either Lesion.*—Of this group of six cases recorded in Table VIII, five were frankly decompensated. Although in Case 28 the patient had a regular rhythm, he improved under rest and digitalis to the point where he was able to get about. His liver receded completely. At the time of the determinations he was still in cardiac insufficiency. But like Case 26 already referred to, he showed normal blood-flow values. Findings in Cases 29, 30, 31, 32 agreed with previous findings in decompensated cases. The latter two, both fibrillators, were fully under the influence of digitalis when examined. The response to the drug was not complete. One was confined to bed, the other was semi-ambulant. Blood-flow measurements reflected this borderline state. There was a reduced stroke volume and an elevated arteriovenous oxygen difference. In Case 33 the patient, who gave no evidence of cardiac failure but suffered from subacute bacterial endocarditis, showed normal blood-flow findings in all respects except the pulse rate.

8. *Hypertension, Cardiac Hypertrophy.*—In this group of 9 cases charted in Table IX our main interest was to determine whether an hypertrophy of the heart uncomplicated by valvular lesions resulted in a greater stroke volume. There were 4 cases of essential hypertension (Cases 35, 36, 42, 43) and 4 cases of hypertension associated with glomerulonephritis (Cases 34, 37, 40, 41). One was a case of unknown etiology. Left ventricular enlargement was a feature of all. Two patients (Cases 34, 41) showed a diminished blood flow similar in magnitude to that found in cardiac insufficiency, although neither had the symptoms and signs of congestive failure. Both patients, however, were in the terminal stages of uremic intoxication, one with a pericarditis and the other ending fatally the following day. Two other patients (Cases 38 and 40) showed evidence of renal insufficiency, but they were both still in good clinical condition. Their blood flow was altogether normal. The other patients, with the exception of Case 42, showed no special clinical features, and the blood flow was within normal limits. In Case 42 the patient was in definite cardiac decompensation with a slow sinus rhythm. Although the stroke volume and index were only at the lower edge of normal, the elevated arteriovenous oxygen difference gave quantitative evidence of the tax on this reserve of the circulation. All factors considered, there seems to be no definite indication of an association of an increased blood flow with cardiac hypertrophy.

TABLE VIII

COMBINED MITRAL STENOSIS AND AORTIC INSUFFICIENCY, NEITHER LESION PREDOMINATING

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
12/ 3/27	Case 28 W. L.	5.2	285	7.7	122	63	1.4	3.7	Preliminary period. Sinus rhythm
		5.6	316	8.5	126	67	1.5	3.7	
12/ 5/27		5.2	292	7.8	118	66	1.5	3.8	
		5.6	289	8.2	110	74	1.8	3.5	
				8.0	119	68	1.6	3.7	Averages
12/14/27		5.4	282	7.5	92	81	1.8	3.8	Received 16 c.c. tincture digitalis
		5.4	262	8.4	85	99	2.2	3.1	day before
12/19/27		5.5	259	7.2	92	78	1.7	3.6	6 days after
		5.5	237	7.0	92	76	1.7	3.4	
1/ 9/28		5.5	265	6.7	100	67	1.5	3.9	25 days after
		5.4	270	6.9	96	72	1.6	3.9	
1/16/28		5.4	280	7.0	92	72	1.6	4.0	32 days after
4/ 6/28	Case 29 S. J.	5.1	229	3.9	94	42	0.82	5.8	No digitalis
		5.1	253	4.1	90	45	0.89	6.2	
1/27/28	Case 30 R. R.	4.9	192	4.0	82	49	1.1	4.8	No digitalis
7/18/28	Case 31 H. Z.	4.9	290	4.9	88	57	1.1	5.9	Received 2 c.c. tincture digitalis
		5.1	261	4.6	76	60	1.2	5.7	daily for 2 months
7/27/28		5.4	251	4.4	68	64	1.2	5.8	Auricular fibrillation
		5.0	257	3.7	66	56	1.1	6.9	
7/21/28	Case 32 S. S.	3.7	247	4.8	88	54	1.0	5.2	Fully digitalized
		3.7	222	4.7	82	57	1.1	4.8	Auricular fibrillation
7/23/28		4.9	254	4.8	84	58	1.1	5.2	
		4.9	240	4.3	71	60	1.1	5.6	
8/27/28	Case 33 P. A.	4.7	229	8.2	104	79	1.6	2.8	Subacute bacterial endocarditis
		4.8	227	8.2	105	78	1.6	2.8	

TABLE IX

HYPERTENSION; CARDIAC HYPERTROPHY

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4/ 4/28	Case 34 Y. W.	4.8	144	4.5	120	37	0.86	3.2	Azotemia. Pericarditis. Uremia
1/11/28	Case 35 M. H.	5.8 5.4	269 222	7.8 6.4	108 97	72 66	1.2 1.1	3.5 3.5	
6/ 1/27	Case 36 B. B.	5.0	271	6.8	82	84	1.1	4.0	
5/20/27	Case 38 R. L.	4.9 4.8	202 209	10.1 8.5	90 87	112 99	2.1 1.9	2.0 2.5	Azotemia. Pericarditis. Uremia
3/30/27	Case 39 M. G.	5.3 5.1	268 240	9.6 8.6	71 71	135 120	1.8 1.6	2.8 2.8	
2/17/28	Case 40 R. B.	4.9 4.8	219 216	6.5 6.3	77 72	85 88	1.4 1.4	3.3 3.4	Azotemia. Renal insufficiency
3/ 2/28		5.2	249	6.3	71	89	1.4	3.9	
1/28/28	Case 41 S. G.	4.5 4.5	265 267	3.6 3.6	107 102	33 35	0.56 0.59	7.4 7.5	Azotemia. Uremia. Died following day
1/19/28	Case 42 J. R.	4.1 4.1	282 254	5.7 6.0	74 59	77 100	1.1 1.5	5.0 4.3	
4/11/28		5.2 5.4	366 245	5.6 4.9	72 60	77 81	1.1 1.2	6.6 5.0	
5/17/27	Case 43 L. P.	5.7	239	10.1	102	99	1.5	2.4	

TABLE X

ARTERIOSCLEROTIC HEART DISEASE; HEART-BLOCK

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4/18/28	Case 44 W. S.	4.1	368	4.7	97	48	0.67	7.8	
		4.0	259	5.0	90	56	0.77	5.1	
3/29/27	Case 45 M. B.	5.3	234	5.3	69	77	1.3	4.4	
7/16/28	Case 46 L. R.	5.4	275	6.5	95	68	1.2	4.3	Fully digitalized. Sinus rhythm
		5.2	239	6.5	95	68	1.2	4.0	
7/17/28		5.4	291	6.6	94	70	1.2	4.4	
		5.7	282	6.7	91	75	1.3	4.3	
9/ 5/28		4.5	325	4.9	109	45	0.78	6.6	Off digitalis for 48 days
		4.6	287	4.7	104	45	0.78	6.6	
5/10/27	Case 47 H. S.	5.1	298	11.5	98	118	1.4	2.6	Preliminary period. Auricular fibrillation
5/11/27		5.3	290	9.4	95	99	1.2	2.3	
5/13/27		5.4	340	8.7	82	106	1.2	3.9	Received 15 c.c. tincture digitalis
5/16/27		5.3	175	7.6	75	102	1.2	2.3	
5/18/27		5.1	207	7.4	65	116	1.3	2.8	
10/13/27		5.4	324	8.0	80	100	1.1	4.0	1 c.c. digitalis daily for months
10/14/27		5.5	324	6.9	76	91	1.0	4.7	
10/18/27		5.3	300	7.8	84	93	1.0	3.9	
10/12/27	Case 48 D. L.	5.1	253	4.6	130	36	0.55	5.6	Preliminary period. Auricular fibrillation
		5.0	250	4.2	128	33	0.51	6.0	
10/17/27		5.0	155	3.3	104	32	0.51	4.8	Received 21 c.c. tincture digitalis in past 48 hours
10/18/27		5.0	164	4.5	96	47	0.73	3.7	
10/19/27		5.2	202	3.5	92	37	0.58	5.9	
2/21/26	Case 61 H. L.	6.0	178	3.6	44	82	2.1	5.0	Complete heart-block
		6.0	203	3.9	45	86	2.2	5.2	
3/30/26	Case 62 I. A.	3.8	320	5.2	28	188	2.7	6.1	Complete heart-block Auricular fibrillation
2/25/26	Case 63 M. L.	5.2	221	5.9	40	146	2.6	3.8	Complete heart-block

TABLE XI

SYPHILITIC HEART DISEASE; ANEURYSM; CONGENITAL HEART DISEASE; MISCELLANEOUS CONDITIONS

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4/20/28	Case 49	4.9	239	5.4	75	71	1.4	4.5	Syphilitic aortitis with aneurysm
	N. R.	4.8	205	5.0	72	69	1.3	4.1	
5/ 3/28		4.6	228	5.1	74	68	1.3	4.5	
		4.8	218	5.0	72	69	1.3	4.4	
7/26/28	Case 50	4.9	312	7.9	85	94	1.4	4.0	Syphilitic aortitis with aneurysm and aortic insufficiency
	J. Y.	5.0	266	7.2	80	90	1.4	3.7	
7/27/28		5.2	295	7.6	78	98	1.5	3.9	
		5.0	285	7.9	77	102	1.6	3.6	
7/23/28	Case 51	5.0	274	5.8	89	65	1.4	4.7	Syphilitic aortitis with aneurysm
	A. K.	5.1	255	5.0	80	62	1.3	5.1	
4/20/28	Case 52	4.2	272	5.0	103	48	1.2	5.5	Congenital heart defect
	L. W.	4.0	282	4.5	97	46	1.1	6.3	Pulmonic stenosis
5/ 2/28		4.3	182	4.0	91	44	1.1	4.5	
		4.0	218	3.8	88	43	1.1	5.9	
4/24/28	Case 53	3.3	220	3.8	98	39	0.97	5.8	Congenital heart defect
	D. P.	3.3	191	3.5	90	38	0.96	5.6	Pulmonic stenosis
11/23/26	Case 54 R. S.	3.2	216	3.1	105	30	0.70	7.0	? Congenital heart defect

TABLE XI—CONT'D

DATE	NAME	ALVEOLAR CO_2 PER CENT	OXYGEN CONSUMPTION C.C. PER MINUTE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
1/28/27	Case 55 F. B.	5.4 5.5	249 221	7.6 6.6	89 83	85 79	1.5 1.4	3.3 3.4	Congenital heart defect Patent ductus arteriosus
10/17/26	Case 56 M. H.	4.7	213	4.7 4.8	86 80	55 60	1.5 1.6	4.5 4.5	Congenital heart defect Patent ductus arteriosus
10/20/26		4.7	212	5.5	80	69	1.8	3.8	
12/29/27	Case 57 M. G.	4.2 4.2	306 328	5.4 5.6	97 98	56 57	0.82 0.83	5.6 5.8	Tuberculous pericarditis Cardiac insufficiency
3/29/28	Case 58 S. M.	4.7	419	7.1	121	58	0.95	5.9	Graves' disease
3/31/28		4.8 5.3 4.9	385 362 405	7.4 7.7 7.4	132 120 125	56 65 59	0.92 1.06 0.97	5.2 4.7 5.5	
	Case 59 K. S.	4.2	194	4.7	94	50	1.23	4.1	Primary anemia
5/11/28	Case 60 L. A.	5.4	313	7.8	103	75	0.91	4.0	Secondary anemia
5/12/28		5.5 5.4 5.2	320 320 305	8.0 7.8 8.2	102 101 100	79 77 82	0.95 0.93 0.99	4.0 4.1 3.7	

9. *Arteriosclerotic Heart Disease. Heart-block.*—In this group charted in Table X we had 5 cases showing various lesions of arteriosclerotic heart disease and 3 cases of heart-block presumably on the same basis. In cases 44, 45, 46 the patients showed electrocardiographic evidence of myocardial degeneration. In Case 45 the patient had a sinus rhythm and no symptoms of cardiac failure. He showed a practically normal blood flow. In Case 44, patient also had a sinus rhythm but was definitely decompensated. His blood flow showed all the features characteristic of this condition. Case 46 was similar to the latter but in addition the heart was fibrillating. When fully digitalized, his blood flow was within normal limits, but when experimentally taken off digitalis his pulse rate rose, the stroke volume and index declined markedly and the arteriovenous oxygen difference increased beyond normal. In short, he presented the typical quantitative features of cardiac failure. Patient 47 had fibrillation and chronic decompensation. She had been partly under digitalis when she arrived at the hospital, where she was under observation for over six months. During this period she was kept more or less fully digitalized. Under these conditions the blood flow figures were found to be at the lower level of normal. Case 48 showed rapid auricular fibrillation. The patient did not respond to digitalis and succumbed some months later. He too showed widely abnormal measurements of the circulation typical of a failing heart.

Patients 61, 62, 63, suffered from heart-block with complete dissociation. None showed clinical signs of cardiac insufficiency and all were ambulant. The chief quantitative finding was the strikingly increased stroke volume and index. This was the only type of case that showed this feature in our whole series.

10. *Syphilitic Heart Disease. Aneurysm. Congenital Heart Disease. Miscellaneous Conditions Affecting the Heart.*—The data on these miscellaneous cases are charted in Table XI. Patients 49, 50, 51 had definite symptoms and x-ray evidence of aneurysm. Aortic insufficiency was also present in Patient 50. Although the lesions were anatomically advanced in all three, the circulation was perfectly sufficient. The reserve factors of the circulation were all within normal limits by an ample margin.

There were 5 cases in this group classed as congenital hearts. Patients 52 and 53 were very definitely such from the signs, x-ray findings and clinical courses. Although not suffering from congestive failure strictly speaking, they presented marked symptoms as a result of their pulmonic artery stenosis. The former was complicated by tuberculosis. The pulse was raised, the stroke index was below normal, and the arteriovenous oxygen difference was markedly elevated. The diagnosis in Case 54 was debatable as to the congenital origin. There were

TABLE XII

SUMMARY OF EFFECT OF DIGITALIS ON CASES WITH SINUS RHYTHM

CASE NO.	TYPE	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KG.	ARTERIOVENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
4	Mitral stenosis	4.5	92	49	1.7	3.7	No digitalis
		3.8	88	46	1.6	4.2	Digitalized for short period. No effect
5	Mitral stenosis	2.3	133	18	0.63	8.0	No digitalis
		2.5	120	20	0.74	7.6	Digitalized for short period. No effect
6	Mitral stenosis	4.0	74	54	1.2	5.8	No digitalis
		4.0	73	56	1.2	6.3	Digitalized for short period. No effect
19	Aortic insufficiency	5.0	111	46	1.5	3.7	No digitalis
		5.6	112	50	1.6	3.3	Digitalized for short period. No effect
20	Aortic insufficiency	5.3	90	59	1.5	4.3	No digitalis
		4.8	82	60	1.5	4.8	Digitalized for short period. No effect
21	Aortic insufficiency	7.3	93	77	1.6	4.1	No digitalis
		7.4	103	72	1.5	3.9	Digitalized for short period. No effect
22	Aortic insufficiency	5.3	63	83	2.3	4.0	No digitalis
		5.4	58	93	2.4	3.4	Digitalized for short period. Doubtful effect
28	Mitral stenosis. Aortic insufficiency	7.5	107	69	1.6	3.8	No digitalis
		7.5	90	85	1.9	3.5	Digitalized for short period. Doubtful effect
46	Arteriosclerotic heart disease	4.8	106	45	0.78	6.6	No digitalis
		6.6	94	70	1.2	4.3	Digitalized for long period. Marked effect

clear signs of congestive failure, however, and the measurements of the circulation were in agreement with this state. Patients 55 and 56, without symptoms and in good health, probably had patent ductus arteriosus. The circulation in both was perfectly normal.

The remaining 4 cases were of mixed varieties. Case 57 was one of active tuberculosis with congestive heart failure resulting from advanced tuberculous adhesive pericarditis. The factors of the circulation were affected in a manner characteristic of heart failure.

Case 58 was one of advanced Graves' disease. The metabolism was much elevated during the determinations, from plus 50 to 85 per cent. This increased oxygen consumption was not met with an increased blood flow, but rather by a greater utilization of arterial oxygen. The stroke volume was below normal; and although it seems more reasonable to interpret it as a result of the tachycardia rather than of an essential decline in cardiac output, it nevertheless indicates poor heart action. As Henderson[3] has shown, an increased demand on the circulation is met in healthy subjects by a steady or increasing stroke volume in spite of the rapid rate.

Two cases of anemia, one primary (Case 59) and one secondary (Case 60), showed no notable features.

11. *Influence of Digitalis Therapy.*—How digitalis brings about improvement in heart failure is still uncertain. Graphic methods have given conclusive data on the action of the drug on the conductive system. Hence, where advantageous changes in rate and rhythm are factors in improvement, the rôle of digitalis is understood. But largely for lack of methods of direct investigation, the action of digitalis is still obscure in those cases where its use is beneficial without primarily affecting the rate or rhythm.

Clinical writers have long adopted the idea that digitalis increases the output of the heart and explained its favorable action in heart failure by assuming a restoration of a diminished blood flow to normal levels. Recent studies by means of x-ray and blood-flow measurements have thrown doubt on this attractive conception. Harrison and Leonard[7] have found in short experiments that digitalis decreases the blood flow in normal dogs. Burwell, Neighbors and Regen[8] report similar findings in normal human beings. Cohn and Stewart[9] have shown too that the early action of digitalis results in a diminished output of the heart but that this effect is later overcome by the greater contraction of the heart muscle when an increased blood flow follows.

From the measurements we have made on the quantitative factors of the circulation in our cases of heart disease, we may analyze the action of digitalis more directly than has hitherto been possible under clinical conditions. Twenty-three cases of our series received digitalis experimentally or as part of their treatment in the wards. Of these, nine had

a sinus rhythm and fourteen were cases with auricular fibrillation. In Tables XII and XIII we have summarized the data given in full in the earlier tables.

Unless otherwise stated the cases were rapidly digitalized with body-weight doses of the tincture of digitalis (1.5 minims per pound). When no more than this quantity was given, it is referred to in the tables as "digitalized short period." When the administration of digitalis was continued in maintenance doses after the initial rapid digitalization, it is referred to as "digitalized long period." Those cases that received less than body-weight doses are referred to as "partially digitalized."

In none of our cases of chronic rheumatic cardiovalvular disease with a sinus rhythm was the administration of digitalis accompanied by any clinical improvement. In Cases 4, 5, 19, 21, in which electrocardiograms were taken, the T-waves promptly became negative in two or more leads, indicating that the drug was actively absorbed.

In agreement with the clinical observations reference to Table XII reveals no definite or consistent change in the quantitative factors of the circulation as a result of the administration of digitalis. With the possible exception of a variable tendency to reduce the pulse rate slightly, the influence of digitalization in Cases 4, 5, 6, 19, 20, 21, was not detectable. Of this series Case 5 only was decompensated. Although there was some increase in the stroke volume as a result of the reduction in pulse rates in both Cases 22 and 28, we must regard these as exaggerated day-to-day variations in cases of aortic insufficiency with unusually large stroke volumes, rather than a significant digitalis effect. This view is supported by the absence of electrocardiographic evidence of digitalis action in both cases.

The only one in our series of subjects with sinus rhythm which was definitely influenced by digitalis was Case 46. The patient was markedly decompensated, on admission, with dyspnea, edema, a large liver, and gave electrocardiographic evidence of myocardial degeneration. He improved under digitalis therapy and diuretics. The blood flow at this time was well within normal limits except for a pulse rate of 94. Digitalis was experimentally withdrawn, and the symptoms of heart failure returned. The pulse rate and arteriovenous oxygen difference rose, and the minute volume, stroke volume, and stroke index fell to levels characteristic of cardiac decompensation. Whether this finding is exceptional or characteristic of the action of digitalis in decompensated cases of arteriosclerotic heart disease with sinus rhythm, we are not in a position to say.

The improvement of cases with auricular fibrillation under the action of digitalis is a common clinical experience. Whether this is brought about through the effect of the drug on the restoration of a normal rate, or an increase in the stroke volume, or both, has never

TABLE XIII

SUMMARY OF EFFECT OF DIGITALIS ON CASES WITH AURICULAR FIBRILLATION

CASE NO.	TYPE	BLOOD FLOW LITERS PER MINUTE	APICAL RATE PER MINUTE	RADIAL RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT (APICAL)	STROKE VOLUME C.C. PER BEAT (RADIAL)	STROKE INDEX C.C. PER BEAT PER KG. (APICAL)	STROKE INDEX C.C. PER BEAT PER KG. (RADIAL)	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
7	Mitral stenosis. Marked decompensation	3.9	91		42		0.92		6.3	Partially digitalized. Slight effect
8	Mitral stenosis. Moder. decompensation	5.6	63		87		1.1		4.7	Fully digitalized. Definite effect
9	Mitral stenosis. Moder. decompensation	5.8	86	79	68	74	1.2	1.3	4.3	Partially digitalized. Definite effect
10	Mitral stenosis. Marked decompensation	3.9	120	106	33	37	0.65	0.73	6.3	No digitalis
		3.7	96	90	38	41	0.74	0.82	5.9	Digitalized short period. Slight effect
11	Mitral stenosis. Moder. decompensation	3.5	103	90	34	39	0.98	1.1	6.3	No digitalis
		4.0	92	88	42	45	1.20	1.3	4.8	Digitalized short period
		4.2	65	65	65	65	1.9	1.9	4.3	Digitalized long period. Marked effect
12	Mitral stenosis. Marked decompensation	4.5	114	100	41	45	1.1	1.2	5.1	No digitalis
		4.7	97	93	48	50	1.3	1.4	4.7	Digitalized short period
		4.8	67	67	72	72	1.9	1.9	4.2	Digitalized long period. Marked effect
13	Mitral stenosis and aortic insufficiency. Marked decompensation	3.6	126	116	29	32	0.79	0.88	5.4	No digitalis
		3.7	89	83	41	44	1.1	1.2	4.9	Digitalized short period
		4.0	67	67	60	60	1.5	1.5	4.3	Digitalized long period. Marked effect

TABLE XIII—CONT'D

CASE NO.	TYPE	BLOOD FLOW LITERS PER MINUTE	APICAL RATE PER MINUTE	RADIAL RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT (APICAL)	STROKE VOLUME C.C. PER BEAT (RADIAL)	STROKE INDEX C.C. PER BEAT PER KG. (APICAL)	STROKE INDEX C.C. PER BEAT PER KG. (RADIAL)	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD	REMARKS
14	Mitral stenosis and aortic insufficiency. Marked decompensation	4.0 3.9 5.0	95 81 79	91 81 79	42 47 64	44 47 64	0.85 0.97 1.3	0.90 0.97 1.3	5.2 4.8 4.3	No digitalis Digitalized short period Digitalized long period. Marked effect
15	Mitral stenosis and aortic insufficiency. Marked decompensation	2.9	64		47		1.1		7.0	Digitalized long period. Definite effect
16	Mitral stenosis and aortic insufficiency. Moder. decompensation	4.5	80		54		1.1		6.4	Digitalized long period. Definite effect
31	Mitral stenosis and aortic insufficiency. Marked decompensation	4.4	74		59		1.2		6.0	Digitalized long period. Definite effect
32	Mitral stenosis and aortic insufficiency. Moder. decompensation	4.6	81		57		1.1		5.2	Digitalized long period. Definite effect
47	Arteriosclerotic. Moder. decompensation	10.4 7.9 7.9	97 74 80		109 108 95		1.3 1.2 1.0		2.5 3.0 4.2	Partially digitalized Digitalized short period Digitalized long period. Diminished effect.
48	Arteriosclerotic. Moder. decompensation	4.3 3.8	129 97		35 39		0.53 0.58		5.8 4.8	No digitalis Digitalized short period. No effect

been demonstrated. Our investigation supplies some data on this point. Cases 11, 12, 13, 14 (Tables IV and V) showed great clinical benefit from prolonged digitalis therapy. The period before digitalis treatment was begun and the period after digitalis was discontinued have been averaged under the identification of "no digitalis" (Table XIII). It will be seen that the measurements of the "no digitalis" period were all abnormal, of the type associated with heart failure. That is, the ventricular rate was high with a large pulse deficit, the stroke volume and stroke index were below the normal range, and the arteriovenous oxygen difference was much elevated.*

The effect of a short period of digitalization was moderate although very definite and consistent. The heart rate was brought down and the pulse deficit reduced; the stroke volume and index were increased; and the arterial oxygen utilization was lowered. After prolonged digitalis therapy, these factors became completely normal showing a total improvement from 50 to 100 per cent.

It must be emphasized that the increase in the minute volume, although definite, was smaller and not in proportion to the change in heart rate and stroke volume. The significance of this will be considered later.

The other cases in our series of auricular fibrillation (Table XIII) support the general findings of the better controlled cases already discussed. Patients in Cases 7 and 10 were very ill (the latter died in the hospital). Both showed but slight clinical improvement on digitalis, and the lack of response was apparent also in the insignificant quantitative changes in the measurement of the circulation. In Cases 8, 9, 15, 16, 31 and 32 we had no determinations before digitalis was given. In spite of the absence of this control it was possible to deduce a definite effect resulting from the administration of digitalis similar in type if not quite the same in magnitude to the controlled Cases 11, 12, 13 and 14. They were of the same clinical types as the latter and responded to treatment in much the same way although not so satisfactorily. A reason for this might be found in the advanced age of this group which averaged over thirty-five years, and hence these patients having suffered from the disease longer may have had less responsive hearts. The significant point, however, remains that the figures for pulse rate, stroke volume and stroke index were very much nearer normal than we had reason to expect them to be if these cases had remained untreated with digitalis. Comparison of these figures with those of untreated cases who were equally decompensated will bring this point out (Cases 3, 11, 12, 13, 14, 29, 46, 48, 57).

*It will be noticed that calculating the stroke volume on the basis of the effective beats (radial rate), the stroke volumes and indexes of these cases although somewhat higher were still definitely abnormal. It cannot be argued that the improvement in these two items which followed the administration of digitalis was only apparent and due to the action of the drug in eliminating the ineffectual beats of the heart as factors in the calculation, since on the corrected basis the improvement was just as striking.

Of the two cases of arteriosclerotic heart disease with fibrillation only one responded satisfactorily. Patient Case 48 was very ill and received no benefit from digitalization. His blood flow showed this too. He died shortly thereafter in the hospital. Case 47 was kept comfortable under digitalis, and her blood flow figures were in agreement with this state.

TABLE XIV

SUMMARY OF QUANTITATIVE FINDINGS IN CASES OF HEART DISEASE COMPARED ON BASIS OF SIMILAR AVERAGE WEIGHTS*

CASES	AVERAGE WEIGHT KILOS	BLOOD FLOW LITERS PER MINUTE	PULSE RATE PER MINUTE	STROKE VOLUME C.C. PER BEAT	STROKE INDEX C.C. PER BEAT PER KILO.	ARTERIO-VENOUS OXYGEN DIFFERENCE C.C. PER 100 C.C. BLOOD
31 Normal cases	64	7.7	79	98	1.55	3.4
	49	*6.0*	79	*76*	1.55	3.4
51 Cases of compensated cardiac disease	55	5.8	81	72	1.40	4.2
	49	*5.5*	81	*68*	1.40	4.2
17 Cases of decompensated cardiac disease	49	4.0	108	38	0.78	6.0
12 Cases of decompensated cardiac disease improved by digitalis	53	5.0	75	67	1.3	4.9
	49	*4.8*	75	*64*	1.3	4.9

*For derivation, see text.

Summary of Quantitative Findings.—In Table XIV we have averaged the results on all our compensated and decompensated cases and compared them with averages on our normal series previously published. In order to make the figures truly comparable it is necessary to deal with subjects that are of about the same weight, since the stroke volume is a function of the weight. Our series of patients included a considerable number of children. Moreover most of the others were in a state of undernutrition so that the average weight proved to be below the normal. We have, therefore, calculated what we might expect the stroke and minute volumes to have been, from the stroke index and ventricular rate experimentally found, employing the lowest average weight of our three large groups as the basis, that is the 49 kilograms of the decompensated cases. Thus if the average weight of the normal group was 49 kilograms, the stroke volume would be 76 c.c. (49×1.55 the stroke index), and the minute volume would be 6 liters (76×79 the ventricular rate). Similarly in the group of compensated cases, the stroke volume would be 68 c.c. (49×1.4), and the minute volume would be 5.5 liters (68×81). These figures appear in italics in Table XIV.

If our cases are divided into three broad groups, a significant comparison becomes at once clear. Those cases of heart disease classed as compensated varied so little from the normal as to warrant no quanti-

tative distinction. The cases classed as decompensated, on clinical grounds, showed a wide quantitative difference from the normal. The minute volume was 30 per cent below the normal, the pulse rate was elevated by 30 beats per minute, the stroke volume was half the normal as was also the stroke index, and the arterial oxygen utilization was almost doubled. The cases that were effectively digitalized, by clinical criteria, showed values that had strikingly returned to nearly normal levels. These changes have a related significance which we may now discuss.

DISCUSSION

This study attempts to contribute to the accumulation of the kind of quantitative data upon which an explanation of the dynamics of cardiac disorders may ultimately be based. Although the necessary data are being gathered from several sources,[9, 10, 11] the sum is still small and too untried from a critical point of view, to warrant extensive interpretations. We cannot, therefore, at this time do more than emphasize what appear to be acceptable facts and indicate the general meaning.

In tracing the physiological implications of our data, it must not be understood that we are offering an explanation of the clinical conditions under discussion, but rather *a picture of what constitutes these conditions in quantitative terms.* Those who, in attempting to corrolate anatomical and clinical findings, have had the common experience of discovering perfectly good heart muscles at the post-mortem table in patients who have died of heart failure, will appreciate the need for distinguishing between the fact and the explanation.

Moreover, it is well to bear in mind the limitation of this study. *We are concerned only with resting subjects.* The circulation is a function with a wide range in responding to normal conditions. In many respects this is its most important quantitative feature. How this range is affected by diseases of the heart is not in the sphere of this study, since our patients could not easily be subjected to the test of effort. The clinical symptoms of dyspnea, fatigability and pain of the compensated cases clearly point, however, to a marked influence in the direction of a contraction of the range of the circulation. With the method of investigation which we have used we get no clue of a departure from normal magnitudes until the heart action has been restricted by disease to the point where it is insufficient for the resting state. This point, it will be recognized, is identical with the clinical condition of heart failure. Hence, when our data disclosed, as we have seen, that the quantitative factors of the circulation were changed only in cardiac insufficiency, it need not be concluded that a decline in these factors did not exist before the phenomena of heart failure appeared. If the circulation had been measured under conditions of effort in the

compensated cases of heart disease, no doubt similar changes might have been brought out. It is possible too perhaps to bring out in this way quantitative differences between the anatomical varieties of heart disease, in which respect our data failed to give any evidence.

The Minute Volume.—The volume of blood flowing from the heart into the arterial system, as has been said, can be resolved into the two factors of the stroke volume and the heart rate. The essentially passive rôle of the left side of the heart in controlling the volume output is commonly lost sight of. It can eject less, but no more, blood than the right heart sends it. The right heart in turn expels a volume of blood determined by the volume of the venous return. What factor fixes the level of the venous return is not definitely known; although there is ground for belief that it is probably more closely related to the need for disposing of carbon dioxide produced, than for the supply of oxygen (since returning venous blood still holds a large reserve of available oxygen). We may be content with the general statement that the metabolic activity is in some manner the determining factor in the volume of venous return. Adopting the accepted practice of expressing metabolic activity by the oxygen consumption, a definite normal relation can be said to exist between the oxygen consumption and the venous return and hence the minute volume of blood flow.

A quantitative expression of this normal relation can be derived from the arteriovenous oxygen difference, which we have seen discloses that from every 100 c.c. of blood flowing from the heart a relatively constant quantity of oxygen is taken away by the tissues under normal resting conditions. It is derived by dividing the minute volume of blood flow stated in deciliters, into the c.c. of oxygen consumed per minute.

Our normal cases (Table XIV) show an average of 3.4 c.c. If we accept 4 c.c. as an average upper normal limit, the relation of the resting oxygen consumption to the resting minute volume of blood flow per unit of time may be expressed in this general way,

$$\frac{O}{V} = 4$$

where O is the oxygen consumption in c.c. per minute, and V is the minute volume of blood flow in deciliters.

It will be readily admitted that whatever the state of health of the circulatory apparatus, metabolism goes on. The resting oxygen consumption cannot diminish. O, therefore, may be regarded as constant, and whatever variations in the quotient $\frac{O}{V}$ appear in heart disease must therefore be attributable to a change in the variable V. The possibility of an increase in V seems remote, for with a constant oxygen consumption there is no stimulus for a larger venous return than obtains normally. As long as the heart action is capable of handling

the venous return called forth by the unchanged oxygen consumption, V will remain undiminished and the quotient $\frac{O}{V}$ will stay at 4. On the other hand, the possibility for a decline in V is strong. If the heart action as a result of disease is not equal to the task of advancing the venous return to the arterial side, V must decline and the quotient $\frac{O}{V}$ will rise above 4. In such an event there must be an accumulation of blood on the venous side, a condition which will clinically be expressed by the phenomena of congestive failure. The degree to which the heart fails in advancing the venous return will be expressed by the degree of rise in the quotient $\frac{O}{V}$.

It is significant, therefore, that in our cases of cardiovascular disease classed as compensated, that is having no clinical evidence of congestive failure, the arteriovenous oxygen difference or $\frac{O}{V}$ quotient was found to be 4.2, a difference from the normal so small that no significance can be attached to it. This means that the minute volume was in practically normal relation to the oxygen consumption, or again that the venous return was completely advanced to the arterial side, and hence there was no accumulation of blood on the venous side. In other words, since the minute volume found (Table XIV) was 5.5 liters, we may assume that the venous return was of this order.

On the other hand, in our cases of cardiovascular disease classed as decompensated, that is having abundant clinical evidence of congestive failure, the arteriovenous oxygen difference or $\frac{O}{V}$ quotient was found to be 6. This means that the minute volume was not in normal relation to the oxygen consumption, or again that the minute volume was less than the venous return, and hence there was a detectable accumulation of blood on the venous side. In point of fact the minute volume (Table XIV) was found to be 4 liters as compared with a probable venous return of the order of 5.5 liters.

Stroke Volume.—In accounting for the failure of the heart to advance the venous return completely to the arterial side, it is necessary to examine the components of the minute volume. We have already seen that the latter is the product of the ventricular rate and the stroke volume, that is to say

$$V = R \times S$$

where R is the ventricular rate and S is the stroke volume.

It follows, therefore, that R and S are inversely related to each other. That is to say, with a constant V, if the rate rises the stroke volume must decline, and if the rate declines the stroke volume must increase. Evidence of the latter we have already encountered in our

cases of heart-block, which showed a very large stroke volume as a result of the low ventricular rate (Table X). The former relation is common even in normal beings[3] when the rate rises through toxic agencies such as tobacco, atropine or mental excitement without physical effort. This dependence of the size of the stroke volume on the rate must necessarily be so, since a more rapid rate will shorten diastole and ventricular relaxation, which in consequence diminishes ventricular filling. This effect will, moreover, be accentuated in cases of mitral stenosis (to which class most of our cases of cardiac insufficiency belonged) on account of the mechanical obstruction to ventricular filling.

This inverse relationship between R and S somewhat complicates the interpretation of changes in the stroke volume S. As long as V remains constant, a decline in S may be attributed to a rise in R. But if V declines along with S, an essential decrease in the stroke volume S must be admitted. And on the other hand, if V remains unchanged, an increase in S may be attributed to a reduction in R, but if V increases along with S, an essential increase in the stroke volume S must be admitted beyond the influence of R.

In Table XIV it will be seen that the average S of our decompensated cases was 38 c.c. This stroke volume was half the output in our normal series and practically half the output in our cases without cardiac insufficiency. We may ask, therefore, whether the markedly diminished stroke volume of 38 c.c. was real or the result of the tachycardia, for in these cases a rapid ventricular rate averaging 30 beats per minute above the normal rate was an almost invariable feature. For, an essential or real diminution in the stroke volume would account for the failure of the heart in these cases to advance the normal venous return to the arterial side, or in other words for the failure of the heart to produce a normal minute volume.

Even allowing for the rapid rate in our cases, an actual decline in the stroke volume must be admitted. It will be seen that the minute volume averaged 4 liters, whereas in the compensated cases it was 5.5 liters and in the normal cases 6 liters. In other words, V decreased along with S, and an essential diminution in the stroke volume in heart failure must, therefore, be a fact. How much of an actual decline there was we can only estimate, but it was certainly not as great as the 50 per cent found.

The significance of the tachycardia is not easy to determine. In the majority of our cases of heart failure auricular fibrillation was a feature, and the elevated R may be attributed to the accident of a disturbed rhythm. On the other hand many cases of cardiac insufficiency with a sinus rhythm show a rapid rate also. It is possible in these cases that the ventricles are not able to accept the burden thrown on them by a slow pulse and that the tachycardia is a necessary compen-

sating effect. It would be interesting to note whether slowing the rate in this type of case by other means than digitalis is well borne.

Digitalis.—If the primary feature of heart failure consists in a diminished stroke volume, we may inquire whether digitalis affects the clinical improvement in these cases through a restoration of a normal stroke volume. We are unable to answer this important question at present with certainty. The interpretation of the data on our cases is still debatable, because the number of cases in which we have well-controlled preliminary periods is small, and we are forced to consider an average effect of digitalis rather than the effect in individual cases. We are reinvestigating this question on a more extended scale and under more guarded conditions.

In only one instance (Case 46), strangely enough with a sinus rhythm, was the increase in stroke volume so large as to be beyond any question of the influence of the slowing in R. In this case V increased along with S by almost 40 per cent.

In Table XIV the effect of digitalis is averaged on twelve cases that had responded with partial or complete clinical improvement. It will be seen the R had been slowed to 75 beats per minute and that S increased to 64 c.c. In spite of the fact that the ventricular rate was even slower than in our normal and compensated heart cases, the stroke volume did not quite reach the S in these cases. The failure of digitalis to bring the stroke volume completely back to normal is not essential, however, to an admission that there was probably a real increase in this factor, since the average includes cases that were only partially improved clinically. Moreover, there was a definite rise in V from the low level found in heart failure, that is the minute volume increased from 4 liters to 4.8 liters, and as we have seen when both V and S increase, the latter is more than an effect of the slower rate. But was the increase in V sufficiently large to be significant?

The average arteriovenous oxygen difference or $\frac{O}{V}$ quotient in the treated cases, including those digitalized with partial and complete effect, was 4.9 as compared to 6 for the untreated cases. The decline in the quotient toward a normal level can be accounted for only by a significant increase in V, since O, the resting oxygen consumption, cannot be considered to have changed. This deduction supports the significance of the rise in the minute volume from 4 liters in the undigitalized cases to 4.8 liters in the treated cases. Incidentally it may be pointed out that the falling $\frac{O}{V}$ quotient also indicates that the heart was advancing the venous return more completely to the arterial side. This perhaps accounts for the resolution of the phenomena of congestive failure under digitalis therapy.

In the 4 cases that were controlled with measurements of the circulation before digitalis was begun (Cases 11, 12, 13, and 14, Table XIII)

the clinical improvement was very marked. The digitalis effect can be said to have been complete, since the rate was brought down into the sixties. Whereas the stroke volumes increased from 50 to 100 per cent above the untreated levels, the minute volumes were only moderately increased. A significant interpretation becomes difficult. It is impossible to say with conviction that in these 4 cases, our best controlled, the rise in S was significantly beyond the influence of the reduction in R, since V did not increase sufficiently along with S.

In view of these incomplete findings we must postpone a decision as to whether digitalis achieves its clinical benefit from a slowing of the ventricular rate alone or also through an essential increase in the stroke volume.

If digitalis does not restore the minute volume to normal, its effectiveness resolves itself mainly into a shifting of the burden of maintaining an unaugmented minute volume from one cardiac reserve to another, that is from an increased ventricular rate and a low stroke volume, to a slow rate and an increased stroke volume. Although it is difficult to see how the phenomena of congestive failure can be resolved under these conditions alone, the change is not without beneficial clinical consequences. To begin with, from the standpoint of the circulation, a normal minute volume is not absolutely essential, for it can continue to draw on an increased oxygen utilization to discharge its respiratory function completely. This fact is often lost sight of. The circulation even in cardiac failure is performing its function completely but at great effort and expense to its reserves. It cannot be overemphasized that the ventricles are first of all muscles, in whose effective operation rest is the most essential element. As the rate is reduced under digitalis, an improvement in muscular activity of the heart may in time take place. It is quite possible that since whatever increase in stroke volume we found appeared after prolonged digitalis therapy, such improvement was the result of the prolonged rest given to the heart through this undisputed action of digitalis.

The vulnerability of a circulation maintained at the expense of a rapid rate and a high arterial oxygen utilization, although performing its respiratory function completely, must be stressed. For any of the indispensable and ordinary efforts of life, such as turning in bed, taking meals, straining or nervous excitement must tax the reserves to still greater limits. When we consider that the stroke volume has already failed and the ventricular rate and the arterial oxygen utilization are exploited to the limits of efficiency, it becomes clear how full of hazard a circulation achieved at such expense must be. The already weakened ventricles are driven to the limit without proper interval for rest. A reduction of the rate is, therefore, the most immediate agent of relief; and if digitalis does nothing more than that, it accomplishes a great deal. It is putting the heart itself to bed.

SUMMARY AND CONCLUSIONS

The conception of the stroke volume, ventricular rate, and arterial oxygen utilization as reserve factors in the circulation which may be drawn on in effort, is outlined. The extent to which these three reserves contribute to the circulation in normal resting subjects is reviewed.

Data derived from 340 measurements of the circulation on 63 cases of a variety of cardiovascular diseases, by means of the Henderson and Haggard ethyl iodide method is presented.

The influence of pulmonary disorders, such as congestion or hydrothorax, on measurements of the circulation is discussed. From an analysis of measurements of the circulation in 21 cases of pulmonary tuberculosis, it was found that disorders of the lungs did not affect the measurement of the circulation.

Irrespective of the anatomical or etiological variety, the resting minute volume, ventricular rate, stroke volume and arterial oxygen utilization were not significantly different from the normal in cardiovascular diseases without cardiac insufficiency. There was a possible exception to this conclusion in cases of congenital heart disease with pulmonic artery stenosis.

Cases suffering from cardiac insufficiency as judged by clinical criteria, of whatever anatomical or etiological origin, showed a diminished minute volume, an accelerated ventricular rate, a diminished stroke volume and an increased arterial oxygen utilization. A circulation of sufficient magnitude to carry on the internal respiratory function was, however, maintained by the increased use of the two reserves of ventricular rate and arterial oxygen utilization.

Cardiac enlargement, as judged by clinical criteria, was not associated with an increased stroke volume.

In three cases of heart-block there was a markedly increased stroke volume.

The influence of digitalis on 23 cases is described. In 9 cases with a sinus rhythm no beneficial effect on the reserve factors of the circulation was detected, with the single exception of a case of arteriosclerotic heart disease with cardiac insufficiency. In 14 cases with auricular fibrillation and cardiac insufficiency, digitalis restored the ventricular rate and stroke volume to almost normal values, but produced improvement in the minute volume and arterial oxygen utilization to lesser degrees.

The significance of these findings in relation to the dynamics of heart failure and the therapeutic action of digitalis is discussed.

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DISPLACEMENT OF THE LEFT NIPPLE IN MITRAL STENOSIS*

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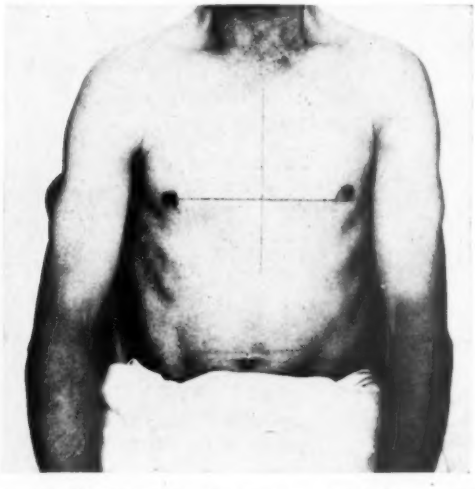
DEFORMITY of the chest in the precordial region, in the absence of disease of the bony thorax is commonly seen in patients with organic heart disease. Indeed, at one time minute mensuration of the chest was practiced with a view of arriving at a diagnosis of valvular heart disease.[1] A correlation of the actual lesions of the heart with such changes in the shape of the chest, however, has never been attempted.



Upward and outward displacement of the left nipple in a man thirty-three years old with mitral stenosis, in whom there were no auscultatory signs of any valvular lesion and in whom fluoroscopic examination revealed a very small heart. The electrocardiogram showed right ventricular predominance with notched P-waves in all three leads.

I have recently been impressed with a deformity in the contour of the chest which seems specific for mitral stenosis. It is the upward and outward displacement of the left nipple which obviously is seen only in children and male adults.

In a group of 200 healthy adult males, I have found the left nipple displaced outwardly in only one individual who had had rickets in early childhood.

In a series of 200 consecutive patients with frank mitral stenosis, 130 adult males and 70 children, varying in age from four to seventy years, I have found this sign positive in over 90 per cent of the cases.

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Of course I have omitted examining any patients with pendulous breasts.

In some of these cases in addition to the outward displacement, I have noted the left nipple to be different from the right in size, shape, and color. In several instances the left nipple was much smaller than the right, the areola was lighter in color and ovoid in contour instead of round.

The following explanation of this phenomenon may be attempted:

With the enlargement of the heart and the increased intra-auricular pressure that takes place as a result of stenosis or damage to the mitral valve, the left auricle dilates and encroaches upon the retrocardiac space. As this chamber dilates, it causes the right ventricle to be pushed forward close to the ventral surface of the anterior chest wall. If the patient is so young that the costosternal junctions are not yet fixed, then the continual pounding of the right ventricle against the anterior chest causes bulging of the cartilage and bones overlying it. A resulting deformity takes place in the region of the mesial left half of the sternum and the adjacent second, third, and fourth costosternal junctions. One severe bout of rheumatic fever in childhood when the chest is still yielding is sufficient to produce this deformity.

The displacement of the left nipple takes place as a result of the adjustment of the muscles and fascia overlying the bulging precordium.

I have not observed this sign in 9 patients with isolated aortic insufficiency or in 10 cases of congenital heart disease.

SUMMARY

In healthy children and in male adults both nipples are usually on the same level. In patients with mitral disease of the heart, who have had rheumatic fever in childhood, the dynamics of the valvular lesion cause a deformity of the chest in the region of the left half of the sternum and the adjacent second, third, and fourth costosternal junctions. Because of this there results an upward and outward displacement of the left nipple. This sign is not present in patients with isolated aortic insufficiency or congenital heart disease. It was present in over 90 per cent of 200 consecutive patients with mitral stenosis examined at the Montefiore Hospital within the last two years.

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MONOPHASIC AND DEFORMED VENTRICULAR COMPLEXES RESULTING FROM SURFACE APPLICATIONS OF POTASSIUM SALTS*

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THE occurrence of monophasic ventricular complexes or of deflections in which the descending limb of R is extended by a rounded hump or merges into a declining plateau has been demonstrated both experimentally and clinically in connection with coronary occlusion followed by infarction. They have been suspected also in association with myocarditis due to rheumatic fever (Cohn and Swift,[1] Porte and Pardee[2]) and have been demonstrated to occur in association with pericarditis and hemopericardium by Katz, Feil and Scott.[3]

While studying the effects of potassium ions upon the intact dog's heart it was found that the intrapericardial injection or localized application of concentrated KCl solutions produced electrocardiograms of a similar nature. The records reproduced as Figs. 1, 2 and 3 are presented as examples of the successive changes found in Lead II. They were recorded by a Victor electrocardiograph arranged to record on a laboratory photokymograph, together with a time record.

Experiment 0-73.—Segment A of Fig. 1 is a control. A 20 per cent KCl solution was applied on the apex of the left ventricle by means of a camel's-hair brush, and Segment B was at once recorded. Segment C was recorded one minute later. Another application was made and three minutes thereafter the curves of Segment D were registered. The heart surface was thoroughly washed with normal saline and three and a half minutes later the record shown in Segment E was taken.

Experiment 0-74.—Segment A of Fig. 2 is a control. B and C were taken one-fourth and one minute respectively after application of 20 per cent KCl solution on several areas of the right ventricle. A further application was made and curves of Segment D were obtained. The curves of Segment E were obtained eight minutes later without wasting the heart.

Experiment 0-70.—Segment A of Fig. 3 is a control. Segment B shows the effect of injecting 4 c.c. of 5 per cent KCl solution into the intact pericardial sac. In addition to characteristic deformation of the ventricular complexes, sinus slowing obtains one minute thereafter. Segment C shows the effects two minutes after injection. After recovery from these effects, the auricle was stimulated by artificial induc-

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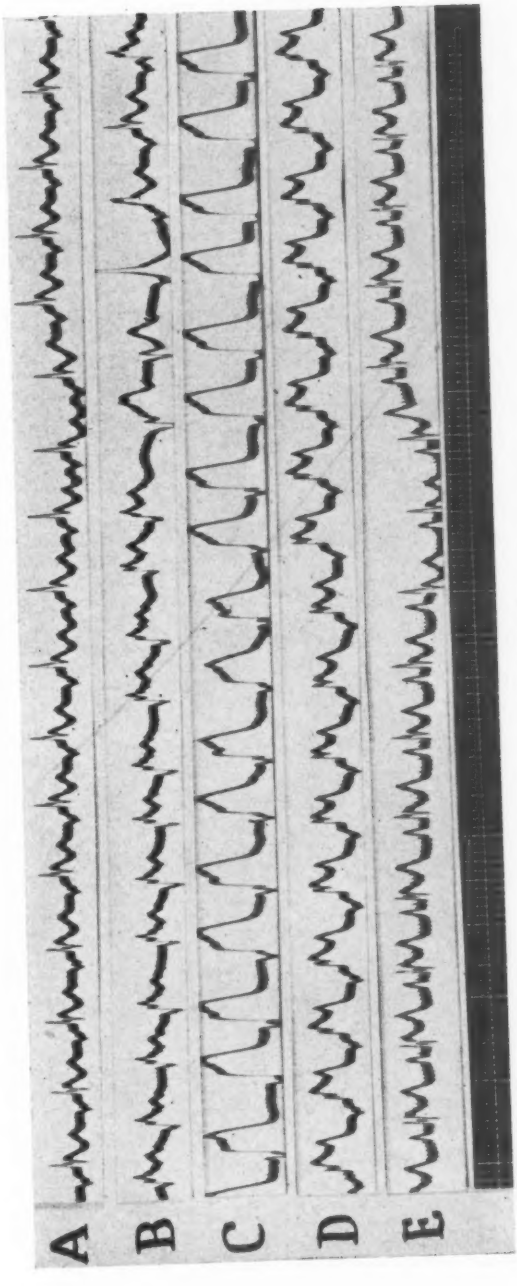

Fig. 1.

tion shocks just discernible as sharp deflections preceding the P-wave in Segment D, which is also a control. Three c.c. of 5 per cent KCl solution was again introduced into the pericardial sac. Records in Segments E and F were taken fifteen seconds and two and three-quarter minutes later. The typical change in the ventricular complexes without change in rate are well shown. The pericardial cavity was washed with saline, and two minutes thereafter the last segment was recorded.

The records require no further discussion, as they speak for themselves.

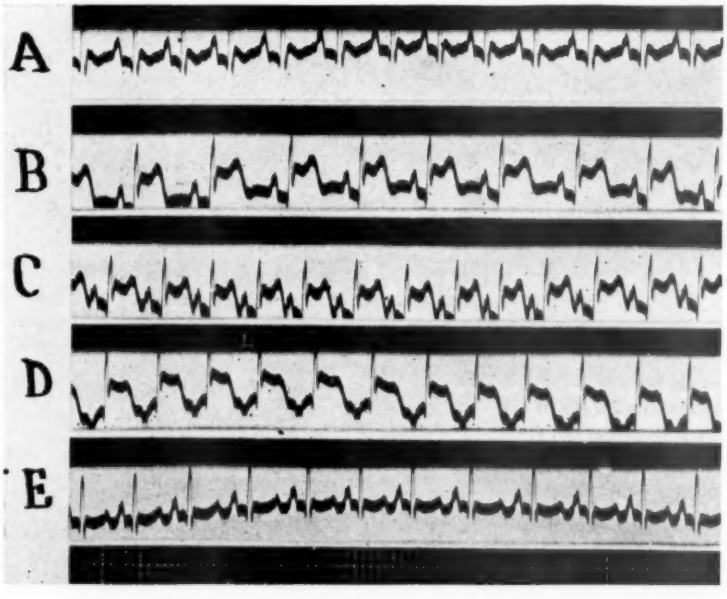

Fig. 2.

The importance of these observations is threefold: First, the fact that chemicals, like potassium, which depress conduction, are capable of producing changes in the electrocardiographic complexes similar to those following coronary obstruction should lead clinicians to temper any diagnosis of coronary disease on the basis of electrocardiographic changes alone. Several other conditions causing depressed conduction may produce ventricular complexes of similar form.

Second, these observations supply the first crucial demonstration that chemicals introduced into the pericardial sac or applied to the surface of the mammalian ventricles are capable of affecting the ventricular beat directly. In 1915, Gunn and Martin[4] professed to have demonstrated such an action, but an examination of their experiments with pilocarpine, adrenalin, etc., by the critical reader will show that

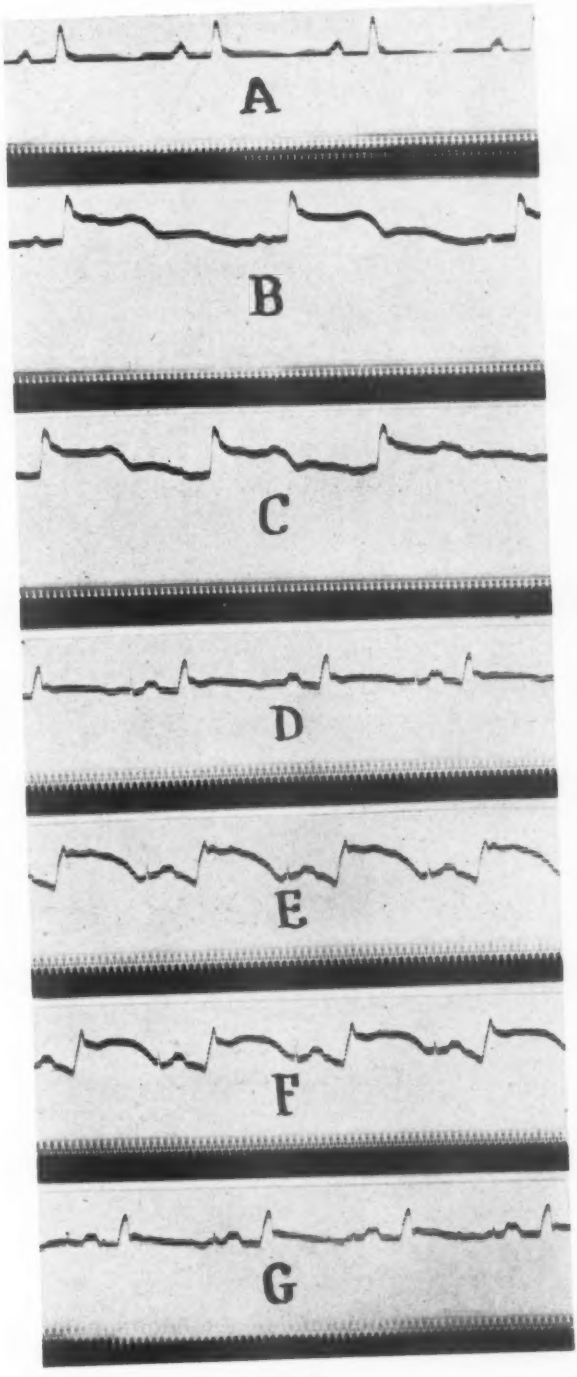

Fig. 3.

they demonstrated only effects produced through auricular absorption and contain no proof that the ventricles were affected otherwise than through secondary changes in rate.

Third, the unsuspected fact that chemical substances are so easily absorbed from the epicardial surfaces is of great clinical interest. It not only opens up therapeutic possibilities but also gives an explanation as to why toxins formed by virulent organisms within the pericardium prove so serious for the ventricle.

SUMMARY

1. It was demonstrated that concentrated KCl solutions applied to the ventricular surfaces or injected into the pericardial sac in small quantities produce either monophasic or deformed ventricular complexes resembling those due to coronary occlusion.

2. Since similar changes in the form of ventricular complexes occur as a result of this and other conditions, caution in the interpretation of such waves is urged.

3. The observations represent the first crucial proof that drugs and chemicals can be directly absorbed from the ventricular surface in mammalian hearts.

4. The therapeutic possibilities are suggested.

5. A logical explanation for the rapid cardiac depression which follows virulent forms of pericarditis is given by these results.

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STUDIES OF VENTRICULAR FIBRILLATION CAUSED BY ELECTRIC SHOCK

II. Cinematographic and Electrocardiographic Observations of the Natural Process in the Dog's Heart. Its Inhibition by Potassium and the Revival of Coordinated Beats by Calcium*†

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(In Collaboration With James R. Bell, M.D., and Margaret Paine)

INTRODUCTION

RECENTLY we[1] reported experiments on the revival of the dog's heart from ventricular fibrillation. Briefly summarized, it was shown that ventricular fibrillation produced by faradic stimulation can be abolished by intracardiac injection of a 5 per cent KCl solution in doses of 1 c.c. per kilogram. Massage was not required in order to produce these effects, but injections into both ventricular cavities appeared to be essential for prompt action. After every trace of fibrillation had disappeared, a subsequent injection into both ventricular chambers of a 5 per cent $CaCl_2$ and 0.1 per cent heparin solution restored a coordinated beat, only, however, when supplemented by cardiac massage.

This paper is chiefly concerned with detailed studies of the fibrillary process, the alterations effected by potassium before complete inhibition occurred, and the mechanisms concerned in revival. Aside from their purely scientific interest, these and subsidiary problems are of practical importance as well, because the basic changes involved in the cardiac mechanism supply scientific proof that the reported resuscitations could by no chance have been a matter of fortunate spontaneous revival.

THE LIMITATIONS AND POSSIBILITIES OF GRAPHIC METHODS APPLIED TO FIBRILLATING VENTRICLES

The hopelessness of following the incoordinate movements over individual portions of the ventricle by inspection has led investigators to adopt myocardiographic and electrocardiographic methods in their study. But the older mechanical methods were often employed without their inadequacy being realized, and the interpretations of electrocardiograms have not always been tempered with the necessary caution.

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†Published by the Physiology Committee on Electric Shock.

In our investigations on ventricular fibrillation, we endeavored to employ the newer aids in graphic registration; hence it was important to orient as to the significance of results that may be obtained by their use.

Accurate mechanical registration of the fibrillating ventricles has proved impossible in the past because efficient and responsive apparatus could not be built. Now that the difficulties in the construction of adequate mechanical recorders have largely been overcome, we are still confronted with the quandary that any mechanical appliance, no matter how efficient or whether it takes the form of surface myograph, cardiometer or intraventricular pressure recorder, constitutes an instrument which records not the ultimate contractions of the ventricle but the resultants of many simultaneous phenomena occurring in successive intervals of time. Our understanding of the intimate nature of ventricular fibrillation has undoubtedly been impeded by our inability to fathom what is taking place in these ultimate fractions of cardiac muscle. The difficulty exists to a certain extent even when the heart is beating in a coordinate manner. Thus, one of us[2] has recently pointed

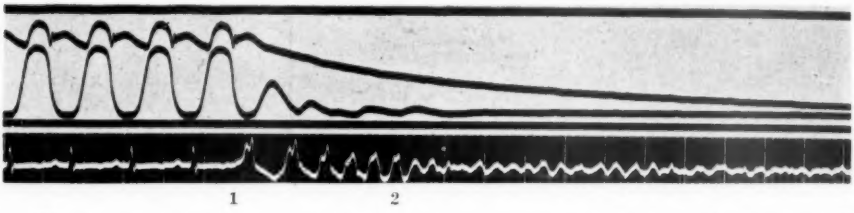

Fig. 1.—Aortic and left ventricular pressure curves and electrocardiogram (Lead II) showing the effects introducing ventricular fibrillation due to faradic excitation. 1 to 2—Initial tachysystole stage. 2 to 3—Stage of consecutive incoordination. Time 0.04 and 0.2 sec.

out that intraventricular pressure curves can be used as graphic evidence as to what the ultimate fractions are doing only because their sequence and orderliness cannot easily be changed under physiological experimental conditions. When, as apparently occurs in fibrillation, the excitation is irregular, disordered and unpredictable from moment to moment, intraventricular pressure curves give no direct evidence as to the character of the fibrillary process. Their value in understanding the mechanisms of fibrillation is only indirect in nature. We may illustrate our meaning by an actual observation: The intraventricular pressure curves of Fig. 1 show that after induction of fibrillation the intraventricular pressure curves alter to a remarkable degree. The pressures which normally varied between 5 and 100 mm. Hg with each cardiac cycle suddenly fall to a mean value of about 10 or 20 mm. Hg. The large, regular, characteristic pressure pulses are replaced by very small, uneven, irregular undulations which bear no direct relation to the fibrillary movements or, as in this instance, by no variations at all.

While it is clear that intraventricular pressure records cannot be

employed to interpret the variations in the strength and frequency of fractionate ventricular contractions, they are of service in another direction. They demonstrate that fibrillation which follows faradic stimulation rapidly passes into such a degree of incoordination that any semblance of regular pressure curves ceases within a second after applying a faradic current. As far as the pressure curves are concerned, the preliminary stage in which a state of tachysystole can be said to exist is extremely short.

Volume curves of the ventricles are of less value than inspection. They show an immediate increase in the size of the heart with the onset of fibrillation, an increase which progresses as fibrillation continues. Inspection gives the same evidence of dilatation but shows in addition that it is due to the predominate dilatation of the right ventricle. Indeed as fibrillation continues, the ballooning effect due to returning blood becomes so extreme on the right side that the left ventricle may have the appearance of a small rounded tumor protruding from the right ventricle. Such an increase in size has frequently been misinterpreted as evidence of an atonic condition of ventricular muscle or of a state equivalent to paralysis. As already pointed out, pressure curves from the left as well as from the right ventricle show that for a long time a pressure range from 10-20 mm. Hg. persists, a finding inconsistent with the idea of atonia. Myographic records from the left ventricle give additional evidence that the mean effect of the fibrillating contraction is to hold ventricular musculature in a position approximately midway between that of systole and diastole. In the right ventricle, however, the venous blood which is pumped into the right ventricle by the continued contractions of the right auricle soon develops sufficient pressure to overcome the tendency to diminish the size of the right ventricle. Moreover, myographic appliances attached to the surface of the heart give no direct evidence as to the character or rate of fibrillary contractions occurring in the ventricle unless they are attached in great numbers and are applied so as to record contractions between points not more than 2 or 3 mm. apart.

With the introduction of the electrocardiograph for practical use, it was generally believed that it offered a method far superior to any mechanical appliance for studying the ultimate character of the fibrillary process. Convenient as the procedure has become, it is not without drawbacks both in its application and in the interpretation of the graphs. When the records are derived by one of the customary three leads, it should be kept in mind that the electrocardiographic oscillations correspond in neither amplitude, regularity nor frequency to the ultimate contractions occurring in any portion of the ventricle. Like the normal electrocardiogram deflections, they represent the first differential quotient of the algebraic sum of potential differences that occur in the heart from moment to moment, oriented in the direction

of the lead. There are these added difficulties in the case of fibrillating ventricles, namely, (1) that the plane of orientation is continually changing as the heart progressively dilates, and (2) that the amplitude and frequency of electrocardiographic deflections due essentially to excitation may not correspond in magnitude or number to the sums of fractionate contractions simultaneously operating in the ventricles.

Studies by Means of Moving Pictures.—These difficulties in the utilization of graphic methods make it necessary to continue placing considerable emphasis upon the description of the incoordinate movements actually witnessed on the surface of the ventricles. As already emphasized, the two chief difficulties in the method of direct observation are (1) the impossibility of noting simultaneously the movements that occur in diverse portions of the ventricular surface and (2) the difficulty of following the extremely rapid movements in any given area. The use of moving pictures taken at close range and at a more rapid speed than that at which they are subsequently projected obviates both of these difficulties and in addition allows considerable magnification of the quiverings occurring in individual areas of the ventricle. Such films or isolated portions of them can be repeatedly thrown upon a screen and reviewed again and again. The observer focuses his attention first upon one and then upon another area or feature of the film itself. By doing this repeatedly in many experiments the authors feel that their conception of the character of the fibrillary process has been greatly extended.

THE NATURAL COURSE OF VENTRICULAR FIBRILLATION

Fibrillation in the anesthetized dog continues from fifteen to fifty minutes (average twenty-four minutes) before complete standstill takes place. The characteristics of the fibrillating ventricles were studied in 18 dogs by taking moving pictures and electrocardiograms during the natural course of such fibrillation.

The method of experimentation was briefly as follows: Dogs were anesthetized with small doses of morphine and sufficient quantities of sodium barbital administered intravenously. The chest was opened, the heart exposed, the pericardium severed and stitched to the lateral walls of the chest so as to form a cradle for the heart. Moving pictures were taken by means of a Bell-Howell camera on 16 mm. film at a rate of 32 exposures per second. The camera supplied with a Zeiss 25 mm. F-2.7 lens was mounted at a distance of 12 to 18 inches from the anterior surface of the heart. Adequate illumination was furnished by three 1000 watt lamps, so that pictures could be taken with the diaphragm stop between 2.7 and 4. Orthochromatic film was used in the first experiments, but great improvement resulted from the subsequent use of panchromatic film. In many experiments, special methods were adopted for locating specific areas upon the ventricular sur-

face. In some cases, small beads were fastened with horsehair by a delicate stitch through the epicardium. In others, white stitches with large knots were similarly placed. In still other experiments, the expedient of thrusting small white-headed pins into the heart itself was tried, and finally the epicardium was bespeckled with small dots of white Duco paint. Finally, good use was made of the reflections of the lamp filaments from the glistening surface of the epicardium. These produced mirror phenomena which frequently brought out the peculiar characteristics of the fibrillating movements to the best advantage.

Coincident with the moving pictures, electrocardiographic records were taken by standard leads. The moments when such records were being inscribed were signalled by a marker operating at the side of the heart. In this way comparisons between the electrocardiographic deflections (usually taken by Lead II) with the actual movements shown in cinematographic records could be made at any time.*

TRANSITIONAL CHANGES IN THE CHARACTER OF FIBRILLARY CONTRACTIONS

From the onset of fibrillation until the ventricles naturally become quiescent, many variations occur in the appearance of the ventricles and in the electrocardiograms. While these changes are transitional in nature, there is sufficient abruptness in the changes to make it permissible for descriptive purposes to divide the course of fibrillation into stages:

(a) The Initial Tachysystolic Phenomena.—Fibrillation of the ventricles usually begins with a very few (2 to 8) peristaltic waves which sweep rapidly over the ventricular surfaces in the general direction of the superficial muscle bundles. Frequently they seem to arise from a single focus located either in the central region or pulmonary conus of the right ventricle and in this case are fairly regular in period and direction. This has been ascertained by counting the number of photographic exposures between the completion of the separate waves. In other cases, however, the waves appear to spread in several directions, beginning sometimes on one area and at other times on several surface regions. The larger contraction waves sweep over both ventricles; e.g., a contraction may originate in the central region of the right ventricle, move in both directions, reaching the base of the right ventricle and the apex of the heart approximately simultaneously; or the wave may start at the pulmonary conus of the right ventricle, sweep over the anterior surface of the right ventricle, apparently hurdle the coronary vessels and pass on uninterruptedly to the left ventricular apex. These first movements are accompanied by character-

*Cinematographic films demonstrating the changes to be described have been exhibited before the American Physiological Society (1928), Cleveland Academy of Medicine (1928), Pacific Northwest Medical Assn. (1928), Buffalo University Medical School Alumni Association (1929), and International Congress of Physiology (1929).

istic deflections in the electrocardiograms which are illustrated in Figs. 1, 2*B*, and 3*A*, between the points labelled 1 and 2. They are of large size, rise and fall rapidly, and occupy an interval of 0.08 sec. or more. Beat by beat their amplitude decreases, their gradients become more gradual, and the periods of the entire beat decrease, i.e., the calculated ventricular rate becomes progressively faster. When the periods are reduced to 0.1 or 0.08 sec., i.e., corresponding if continued to a ventricular rate of 600 to 750 per minute, the process abruptly passes into the next phase.

As shown in Fig. 1, each electrical deflection is accompanied by a small but distinct elevation of intraventricular pressure, though the aortic pressure declines steadily because no blood is expelled. All the evidence, therefore, favors the view that these beats are still coordinated in the sense that they sweep over the ventricles in regular paths and develop sufficient force to elevate intraventricular pressure.

In the dog's heart this tachysystolic stage usually lasts less than 1 second; in fact, it usually sets in before faradic stimulation has ceased. This is not surprising in view of the high contraction frequencies reached.

(*b*) *Stage of Convulsive Incoordination.*—The initial stage already described leads into a second in which waves of contraction with distinctly different rhythms and sequence pass over the ventricles. This stage ordinarily continues from fifteen to forty seconds, but in several instances it was shorter.

When any small circular area 2 to 3 cm. in diameter is carefully observed in projected moving pictures, it can easily be seen that the frequency has increased and that the sequence of contractions is less regular. The localized contractions appear to be rather forceful, but successive contraction waves do not spread over identical paths or involve the same surface groups of muscle tissue. By comparing several such areas, it is noted that the frequencies differ and bear no relation one to the other. Owing to the extreme incoordination, no pressure oscillations occur within the ventricles.

This stage of incoordination is characterized by large, rather violent oscillations of the galvanometer string. They are illustrated in Figs. 1 and 3*B*, between points 2 and 3. In these instances the successive waves vary considerably in contour, amplitude and period, but the frequency, calculated over a considerable portion of the curve, may be placed between 600-660 per minute. Occasionally the electrocardiographic oscillations become even more rapid while this form of incoordination is in progress. This is well shown in Fig. 2*B* between the points 3 and 4 where they attain the alarming frequency of 1,560 per minute. Careful comparisons of electrocardiograms and cinematographic records during such intervals have clearly demonstrated, however, that these rapid electrocardiographic deflections do not portray

the contraction phenomena visible on the surface of the heart, for the latter are always much slower during this stage of fibrillation. In the instance shown in Fig. 2 the stage terminated at point 5.

When the ventricles are held in the palm of the hand, a fluttering, undulatory, convulsive sensation is experienced, no doubt due to the

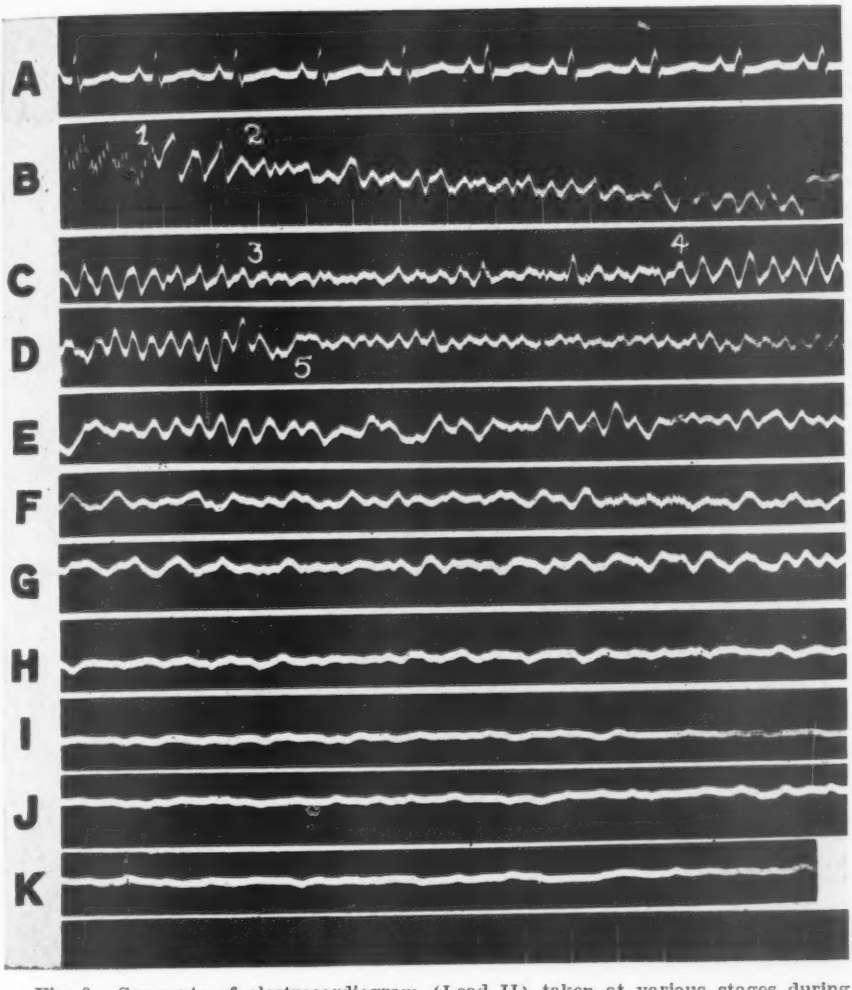

Fig. 2.—Segments of electrocardiogram (Lead II) taken at various stages during the course of fibrillation (043). *A*, control; *B*, and *C*, immediate effects; *D*, after thirty seconds; *E*, after one min.; *F*, after one and one-half min.; *G*, after two min.; *H*, after five and one-half min.; *I*, after sixteen min.; *J*, after twenty min.; *K*, after twenty-one min. Time 0.04 and 0.2 sec.

fact that blocks of myocardium are contracting with different strengths and at different rates and rhythms. From the convulsive appearance of the heart and the fact that no periodic changes of intraventricular pressure are produced, we have designated it as the stage of convulsive incoordination. The terms *coarse fibrillation, flutter, un-*

dulation, ondulation, Wühlen und Wogen, etc., used by others might be applied but are avoided since we are not certain that they were always limited to the particular stage we desire to describe.

(*c*) *Stage of Tremulous Incoordination.*—This type of incoordination ordinarily follows upon the coarse, convulsive type and continues for two or three minutes. The entire surface of the ventricles presents the appearance of multitudes of shivering and shimmering motions of a very rapid sort. The contraction waves spread very rapidly and apparently only short distances. We have seen many instances where reflected light beams from the epicardium give the impression of darting wriggling worms or of contraction waves chasing each other in circles. When the heart is palpated, it gives the impression that has been so aptly described as similar to that obtained when the hand is thrust into a can of worms. This stage is undoubtedly comparable to the types of fibrillation described as *delirium cordis, mouvement fibrillaire, Herz-zittern, fibrillary twitchings,* etc., by others, but for reasons already given we have purposely avoided previously used terms.

Viewed as slow motion picture films, the process is seen to consist of localized contraction waves spreading over short distances or circling around in very limited areas. Their speed of propagation is not actually increased. The frequencies of these visible contractions in different regions of the ventricular surface are apparently unrelated. We have studied one instance carefully in which the rate varied between 600 and 1800 per minute in different portions of the right ventricle. We have tried numerous and laborious expedients for interrelating these rapid contraction circles in selected regions, but after diligent attempts we have found this impossible.

During this stage the electrocardiographic deflections increase in frequency and diminish in amplitude. They are shown in Fig. 2*D* after point 5 where their frequency is about 1140 per minute and in Fig. 3*C* where they average about 1520 per minute. Counts in other experiments give ranges from 1100 to 1700 per minute. Pressure curves recorded from the ventricular cavities show that these rapidly executed incoordinate contractions of extremely small muscle units not only maintain the previous existing intraventricular tension but sometimes actually increase it somewhat. The pressure curves, however, continue as a straight line and show no evidence of oscillations except occasionally those due to continuing auricular contractions.

(*d*) *Stage of Progressive Atonic Incoordination.*—The stage of rapid incoordinate contractions just described is gradually replaced by a stage of coarse atonic incoordination, so designated because the visible waves not only become coarser and slower, but they no longer maintain the previous small even elevation of intraventricular pressure. We are not aware of any previous description of this stage; most observers limiting themselves to the phenomena characterizing the earlier stages.

The ventricular surfaces show characteristic changes in appearance. During the early portion of this coarse atonic stage of fibrillation, wavelets of contraction are seen to spread over small areas of the ventricle. The rhythm is obviously different in different regions. The rate of propagation slows down materially, the frequency of movement is reduced, and the contractions are obviously less vigorous. At first such movements occur over the entire ventricular surface, but gradually they decrease in intensity until certain areas display none. The quiescent areas increase in number until finally only the slightest movements remain in a few regions. The areas which usually pulsate longest in this manner are those which lie near the coronary vessels, usually to the right side of the septal demarcation. The last movements to be seen are mere quivers, perceptible only when beams of light from a lamp are reflected from the moist and glistening epicardium. Frequently, when all visible movement has apparently ceased and no sensation can be felt by the finger or heard on auscultation, the electrocardiograph still continues to show minute irregular oscillations. Whether these are accompanied by contractions in the deeper layers of the ventricle or whether conduction occurs without mechanical shortening under such circumstances, cannot be decided with finality.

The nature of the electrocardiographic oscillations up to the final cessation of all movement is shown in Fig. 2, segments *E* to *K*. At first, the oscillations are fairly large; indeed they resemble those occurring during the early stage of convulsive incoordination. Their frequency ranges from 540 to 720 in Fig. 2. The amplitude of the deflections gradually decreases until toward the end only small oscillations remain. The frequency then also diminishes, e.g., in Fig. 2*K* the frequency is about 360. These changes in rate correspond reasonably well with movements visible in cinematographic records, but obviously the amplitudes of the deflections in the early part of this phase bear no relation to the intensity of fibrillary contractions.

Auricular Contractions During the Course of Ventricular Fibrillation.—The auricles maintain a regular rhythm for a variable length of time. Sometimes their contractions terminate before ventricular fibrillation ceases and at other times they outlast the fibrillation. The changes in the auricles are those common to other forms of asphyxia. The auricular rate soon decreases, the contractions first increase but soon decrease in vigor. It should be borne in mind that the electrical records of ventricular activities may be periodically modified by electrical variations due to auricular contraction. Very early the rate of propagation is reduced. Peristaltic waves sweep over the auricle at slow rates, giving a beautiful visible demonstration of the successive contractions of adjoining fractions. Frequently heart-block develops between the right and left auricles. On several occasions independent rhythms have been observed, suggesting that a rhythmic center becomes active in the left auricle.

THE CHANGES DURING POTASSIUM INHIBITION

The earlier manifestations of fibrillation transpire so quickly that potassium salts cannot be administered easily until the stage of tremulous incoordination has supervened. Cinematographic and electrocardiographic records from eight experiments were carefully studied. They consistently showed that potassium salts do not modify the stages of the fibrillary process; they merely hasten the process. The fifteen to fifty minutes naturally required for fibrillation to run its

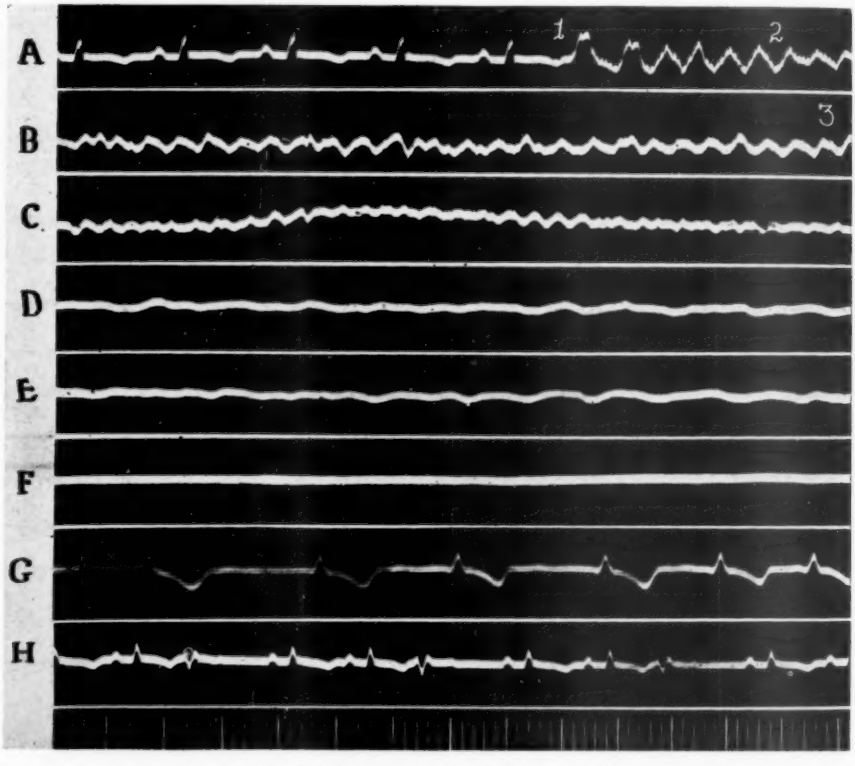

Fig. 3.—Segments of electrocardiogram (Lead II), showing the early stages of natural fibrillation, the effects of KCl and of revival following use of $CaCl_2$ (O-42). *A*, control and initial tachysystolic stage; *B*, coarse incoordination, one and one-half min. later; *C*, tremulous incoordination after two min.; *D*, one min., after use of KCl: *E*, two min. after; *F*, two and one-half min. after; *G*, initial indioventricular beats, recorded nineteen minutes after fibrillation first started; *H*, thirty min. after record *H*. Time 0.04 and 2 seconds.

course are often shortened to one or two minutes. Projected moving pictures show that the fine fibrillary waves in any region recur less frequently and spread more slowly without involving larger areas. On the contrary, the active regions gradually diminish, leaving motionless areas over the entire surface of the heart. The vigor of the localized contractions also diminishes visibly, until large areas are entirely quiescent. Feeble, slow contractions finally remain only in very re-

stricted areas, the anterior region of the right ventricle near the interventricular sulcus being the usual area in which feeble contractions persist longest.

The electrocardiographic curves also reveal no new features, but the entire process normally present runs its course more rapidly. That portion of the atonic stage which is characterized by large deflections is particularly affected. It is either very short or does not appear at all. Fig. 3 is an example of the characteristic electrocardiographic changes. Segments *A*, *B* and *C* illustrate the course of events during the first two minutes of natural fibrillation. The record shown as segment D was taken one minute later, i.e., fifteen seconds after injection of KCl. The records reproduced as segments *E* and *F* were taken at additional intervals of twenty and twenty-five seconds respectively. Almost immediately the amplitude of oscillations greatly diminished and their frequency was reduced to 240 per second in segment *E*. Fibrillation was completely abolished (segment *F*) one minute after completion of the injections.

It should be added that visible auricular contractions which normally persist for many minutes also promptly stopped. The auricles quickly came to a complete standstill. This demonstrates that potassium diffuses quickly through fluids in the cavities of the heart.

THE COURSE OF REVIVAL AFTER USE OF CALCIUM AND MASSAGE

After intraventricular injection of calcium salts and after the ventricles have been massaged for several minutes in such a way that each compression causes a slight elevation of aortic pressure, it is noticed that the ventricles respond to mechanical stimuli or compression. Similar responses may be obtained by gentle taps or single electric shocks. The ventricles recover their functions of conduction and contraction prior to regaining their ability to generate spontaneous impulses. The auricles are not yet contracting automatically; the nodal structures likewise have not regained their automaticity. Within a comparatively short time—a matter of ten seconds in some experiments and one to two minutes in others—spontaneous ventricular beats begin. Projected moving pictures show clearly the broad waves of contraction spreading over the ventricles. Beginning over the central region of the right ventricle they usually sweep upward toward the base of the right ventricle, although downward moving waves of contraction were witnessed in two instances. In the case of the left ventricle, they start at the apex, move upward along the coronary vessels, then to the left and toward the base. One instance was found in which the contraction waves had the ratio of 3:52, but, as a rule, they have the same tempo. The waves appearing over the surface of the two ventricles are not quite synchronous, however, sometimes the right and sometimes the left ventricular waves are in the lead.

As these slightly asynchronous waves gradually become stronger, the ventricles undergo a curious deformation, each beat being not unlike that seen when rapid ventricular tachycardia is produced by stimulating one ventricle artificially. Since each of these contractions elevates mean arterial pressure, it must be accompanied by elevations of intraventricular pressure. Unfortunately, we have not succeeded in recording reliable intraventricular pressure curves of this event.

At the same time that the idioventricular rhythm develops or slightly thereafter, the auricular beats return. Frequently the left auricle beats alone; again both auricles beat at different rhythms; and

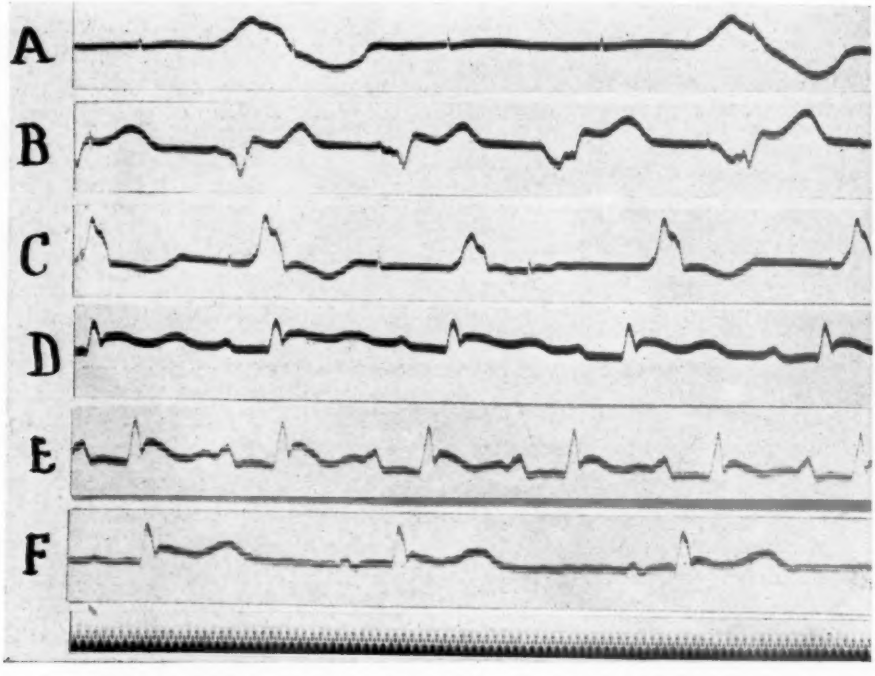

Fig. 4.—Electrocardiograms (Lead II) showing mechanisms in recovery from fibrillation. Description in text. Time 0.02 sec. (O-70, VI-XI).

finally a coordinated rhythm is established. Impulses do not yet reach the ventricles, which continue to beat with an idioventricular rhythm. This is also demonstrated by electrocardiographic tracings. Segment *G* of Fig. 3 shows a series of such idioventricular beats of increasing frequency which were recorded after an initial period of less regular action. They indicate that a single ventricular focus dominates the rhythm. This is not always the case, however, as is shown in the tracings of Figs. 4 and 5. Comparison of segments *A*, *B*, and *C* of Fig. 4 show clearly that the pacemaker shifted. This is partly due to the fact that a more rhythmic center functionates but not necessarily so. Thus the rate was 58 per minute in segment *C* and 120 in segment

B. Dynamically, beats originating in different centers were equally effective, for the blood pressure altered with the heart rate. Frequently, also, successive stimuli arise from different foci; a struggle for supremacy in the idioventricular rhythm apparently takes place. This is illustrated in segments *A*, *B* and *C* of Fig. 5, which show records obtained on recovery from a second fibrillation which had been induced approximately one hour later in the same animal.

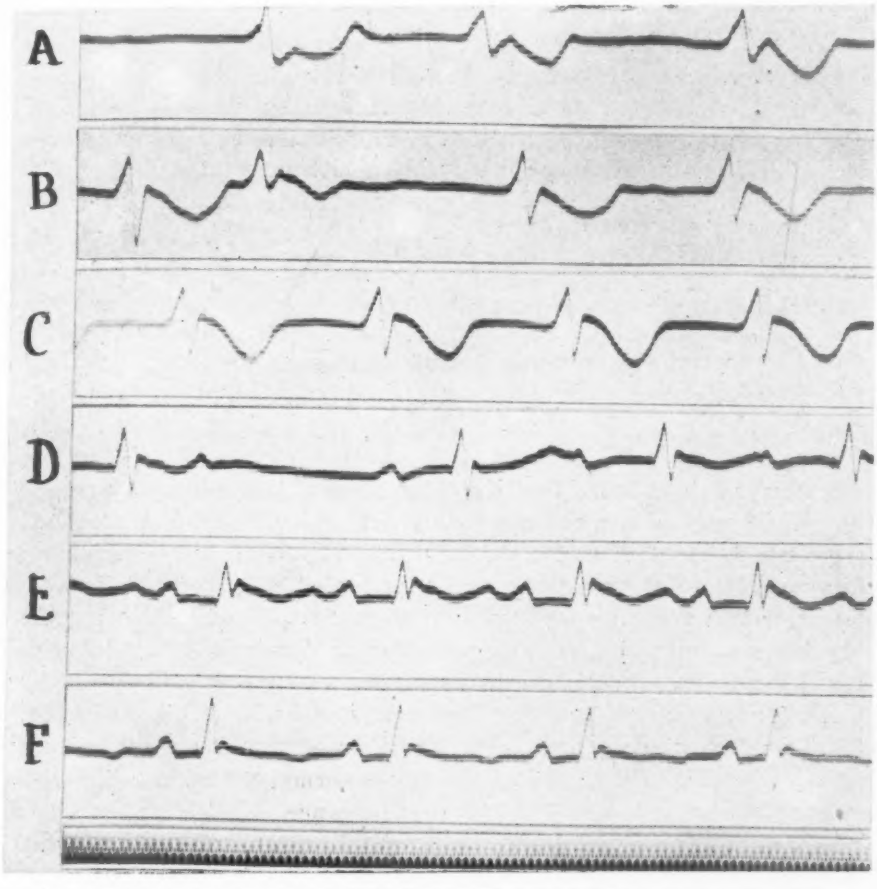

Fig. 5.—Electrocardiograms (Lead II), showing mechanisms of recovery from a second fibrillation in the same dog. Time 0.02 sec. Description in text (O-70, XV-XX.)

The development of this idioventricular rhythm is of greatest importance in tiding the animal over the last few critical minutes still remaining before irreparable damage is done to the central nervous system. It often precedes the redevelopment of a sinus rhythm for the auricles and, at all events, establishes effective beats capable of maintaining a reasonable blood pressure level during the interval that complete A-V block persists.

The fact that revival is inaugurated by an idioventricular rhythm is additional positive evidence that our recoveries were not spontaneous or due to chance. Spontaneous recovery, such as occurs frequently in the cat's heart and occasionally as a special phenomenon in sensitized dogs' hearts, is different in nature. Fibrillation ceases promptly, a long post-undulatory pause follows, and then a regular supraventricular beat reappears immediately.

After revival by calcium, associated with massage, such a rhythm only develops subsequent to an idioventricular rhythm of several minutes' duration. The change in pacemaker is quite abrupt. Previous to its development an auricular beat dominated by the sinus node makes its appearance, auricles and ventricles beating with independent rhythms. Quite suddenly the total block is lifted, and the ventricles begin to beat in sequence with the auricles. The electrocardiographic changes typical of this condition are shown in the lower records of Figs. 4 and 5. The normal P, R and T sequence obtains. The records taken immediately after development of a supraventricular rhythm differ from the normal in several ways. Usually, as in the record of Fig. 5*D*, the P-R interval is prolonged, but this is always reduced to normal values within five or six minutes or less (cf. Fig. 4*F* and Fig. 5*F*). The deflection is often abnormal in contour, reminding one of the variable changes that follow coronary ligation. Frequently the descending level of R does not return to the base line but grades into it by a broad declining plateau or is followed by a rounded hump. These features are often more pronounced than in the case of segments reproduced as Figs. 4*E* and 5*E*. After these abnormalities disappear, the T-wave may become accentuated as in Fig. 4*F*, but frequently it is negative, as shown in Figs. 3*H* and 5*F*. The normal rhythm once regained becomes permanent. A relapse to an idioventricular type was not observed. Not infrequently it is interrupted by premature systoles of auricular, nodal or ventricular origin, as in Fig. 3*H*. Gradually the normal characteristics of the electrocardiogram reappear. The P-R interval is reduced to normal values, and the ventricular waves regain their natural appearance. That the heart has not been injured permanently, either by the concentrated salt solutions employed or by the period of temporary anemia, is thus conclusively established.

SUMMARY

1. The natural course of events from the onset of fibrillation following faradic excitation to complete diastolic rest was studied by recording electrocardiograms and moving pictures simultaneously. In addition, intraventricular pressure curves were optically recorded during a number of experiments. The changes taking place when fibrillation was inhibited by intraventricular injections of 5 per cent KCl and the process of recovery following similar injections of 5 per cent $CaCl_2$

solutions combined with massage, were investigated by the same means.

2. Fibrillation induced by faradic stimulation continues naturally for fifteen to fifty minutes and may be divided into 4 stages, on the basis of surface changes, electrocardiographic deflections and intraventricular pressure variations.

3. The initial stage of tachysystole lasts less than one second and is characterized by the spread of rapidly recurring but coordinated contraction waves, by large electrocardiographic deflections with steep gradients and by definite if small intraventricular pressure variations.

4. The second stage of convulsive incoordination ordinarily lasts fifteen to forty seconds and is characterized by rapid irregular localized contractions which spread short and variable distances over the heart. They are accompanied by large electrical deflections, 600 or more per minute, which vary considerably in size, amplitude and contour.

5. The third stage of tremulous incoordination ordinarily continues two or three minutes and is characterized by multitudes of irregular yet forceful shivering or trembling motions, each spreading very short distances and with highly variable frequencies over different surface regions. They give rise to small irregular electrocardiographic oscillations having frequencies between 1100 and 1700 per minute, and are capable of increasing the intraventricular pressure level slightly.

6. The fourth stage of atonic incoordination is characterized by feeble wavelets of contraction spreading irregularly and at slow rates over small areas until more and more areas become quiescent, and finally the very slightest movements remain in a few areas only. The electrical deflections perhaps become slightly more regular in contour and spacing, but their amplitude becomes progressively smaller, and their frequency is gradually reduced to 400 per minute or less.

7. Potassium chloride injected into both ventricular cavities does not modify the stages through which fibrillation naturally passes; it merely hastens the process so that fibrillation stops within an average period of 2.4 minutes.

8. Intraventricular injections of $CaCl_2$ after potassium inhibition combined with massage, first inaugurate a coordinated idioventricular rhythm, characterized by slow waves of contraction sweeping over the two ventricles asynchronously but in coordinated fashion. After a short interval, a supraventricular rhythm is reestablished, the electrocardiogram regaining all its normal characteristics.

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ELECTROCARDIOGRAPHIC STUDIES BEFORE AND AFTER CHEST OPERATIONS*†

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IN EXTENSIVE operations on the chest possible damage to the heart is of ever present concern to the surgeon. In chest surgery there are the peculiar local factors of displacement, sudden changes in pressure, changes in the pulmonary circulation in addition to the general factors of anesthesia, surgical shock and infection. The ultimate damage to the heart, if any, by these local factors can be determined only by careful clinical observation of the patient during the years following operation.

Some time ago it occurred to us that the immediate displacement of the heart frequently observed following chest operations might have a part in determining either the convalescence or subsequent state of health of the patient. As a possible aid to estimating the effect of displacement on cardiac function, electrocardiographic studies were made on a selected group of twenty-two of the patients admitted to the services of one of us (R. B. B.). Each patient was referred for electrocardiograms before and immediately after operation. Those patients who required multiple stage operations were referred after each operation. X-ray plates of the chest were made before and after each operation.

The results were studied from the following points of view:

1. X-ray evidence of cardiac displacement.

2. Changes in the electrocardiogram which would indicate structural or functional change in the heart.

3. Changes in the electrical axis (which can be interpreted as indicating change in the anatomical axis).

The patients have been grouped according to the type of operation. Some had more than one type of operation. Some had multiple stages of the same operation.

Extrapleural Thoracoplasty.—(Seven cases.) The operation of extrapleural thoracoplasty is performed on patients with unilateral, or virtually unilateral, pulmonary tuberculosis who have not responded to sanatorium treatment. The object is to collapse and immobilize the affected lung. This is accomplished by removing segments of the ribs posteriorly from the 1st to the 11th inclusive. The operation is performed in two or more stages.

*From the Otto Baer Fund for Clinical Research at Michael Reese Hospital.
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In this series four patients had right-sided lesions. In all of these the heart after operation was displaced to the left, according to the postoperative x-ray findings. The extent of displacement varied from slight to moderate. All showed some functional change as evidenced by decrease in amplitude of the R-wave or inversion of the T-wave or both.

One patient, a young woman, developed inversion of the T-wave in Lead II and an increase in the inversion of T-wave in Lead III following the first stage. Following the second stage the inversion was much more marked and was of the coronary type. There was evidence of considerable change in the anatomical axis of the heart, and there were also clinical signs of severe cardiac embarrassment, following the second stage. Displacement of the heart, according to x-ray evidence, was only moderate. Respiratory mobility of the heart was increased slightly after the second stage operation in two cases and remained unchanged in two. The electrical axis changed 32° in the direction of right axis deviation in one patient, and 45° in the direction of left axis deviation in another. In the other two there was no change, or so slight a change as to be within the limits of error.

According to Lewis[1] change in the electrical axis is a rough measure of change in the anatomical axis of the heart. In order to determine accurately any actual change in electrical axis after operation the range of variation in the axis during respiration was measured in each curve before and after operation, and the axis obtained in similar phases of the two curves compared. We may reasonably infer that in two patients there was an appreciable change in the anatomical axis of the heart. The one showing the change of 32° is the young woman referred to above.

Three patients in the group had left-sided lesions. Two showed slight displacement of the heart shadow to the right after operation. One showed slight functional change in the electrocardiogram, the other none. Neither showed structural change. Respiratory mobility was not affected. There was no change in electrical axis in one; in one a change of 10°. The third patient, a man 43 years old, was of especial interest. The electrocardiograms before operation showed evidence of structural damage (low amplitude of QRS in all leads, slight notching of R in Lead II, marked notching of S in Lead III, absence of isoelectric period in the R-T interval in all leads, inversion of T in Lead III, slight notching of P in all leads). This was the only patient showing electrocardiographic evidence of heart muscle damage prior to operation. While the changes were slight, still they were thought to be more than could normally be accounted for by his age. We have seen patients with much more marked electrocardiographic evidence of myocardial damage withstand major abdominal operations without difficulty, yet this patient died of cardiac failure on the fourth postoperative day, after an apparently well-tolerated first stage. We

TABLE I

GROUP I. EXTRAPLEURAL THORACOPLASTY

NAME	AGE	SEX	DIAGNOSIS	SITE	OPERATION	DISPLACEMENT OF HEART SHADOW, BEFORE	SHIFT OF HEART SHADOW, AFTER	RANGE OF ELEC. AXIS, BEFORE	RANGE OF ELEC. AXIS, AFTER	FUNCTIONAL CHANGE	STRUCTURAL CHANGE	RESPIRATORY MOBILITY	ANATOMICAL AXIS
BU	16	F	T. B. hydropneumothorax	R	Aspirated 100 c.c. air 300 c.c. fluid Thoracoplasty 11 – 6 inc.	To left	More to left	+57° to +64°	+63° to +69°	+	None	Same	Slight change
	16	F	Same	R	Aspirated 100 c.c. air 125 c.c. fluid 6 – 1 ribs	Back to previous position	Slight to left	+34° to +52°	+66° to +77°	+	None	Increased	Marked change
FI	22	F	Tbc.	L	Thoracoplasty	None	To right	None to +58°	None to +59°	None	None	No change	No change
	22	F		L	Same 2nd				None to +58°	+	Slight improvement	No change	No change
TR	24	M	Lung abscess. Bronchiectasis	R	Thoracoplasty 1st stage 6 back		To left	+35° to +42°	+39° to +43°	+	More marked	Same	No change
	24	M		R	2nd stage 6 front			+36° to +44°	+34° to +48°	+		Increased	Slight total change
FI	26	F	Tbc. pyopneumothorax	R	Drainage Emp. 11 – 1 ribs	Slight to left	Slightly more to left	+58° to +79°	+69° to +90°	Slight	None	Same	Slight change
BU	21	M		L	7 – 4 ribs		Slight to right	+42° to +49°	+32° to +38°	+	None	Same	Slight change
ST	25	M	T. B. empyema	R	11 – 6 1st stage	None	No x-ray	+65° to +73°	+20° to +30°	+	None	Same	Marked change
	25	M		R	6 – 1 ribs 2nd stage		Left		+37° to +47°	None	None	Same	Moderate change
PA		M			11 – 7 1st	Died cardiac failure 4 P.O. day E. C. G. Subendocardial lesion.							

TABLE I—CONTINUED

NAME	AGE	SEX	DIAGNOSIS	SITE	OPERATION	DISPLACEMENT OF HEART SHADOW, BEFORE	SHIFT OF HEART SHADOW, AFTER	RANGE OF ELEC. AXIS, BEFORE	RANGE OF ELEC. AXIS, AFTER	FUNCTIONAL CHANGE	STRUCTURAL CHANGE	RESPIRATORY MOBILITY	ANATOMICAL AXIS
GROUP II. PHRENICOTOMY													
BR	64	M	Lung abscess	R	Phrenicectomy after pneumo.	None	To left 1 cm.	−53° to −30°	−53° to −30°	None	None	Same	No change
TR	23	M	Lung abscess. Bronchiectasis	R	Phrenicectomy after thoracoplasty	None	None	+34° to +48°	+39° to +48°	None	Improvement	Sl. less	No change
PR	24	F	T.B.C. L. lower	L	Phrenicectomy	None	Very little to right	+26° to +36°	+14° to +19°	None	None	Less	Change
WO	29	M	Bronchiectasis	R	Phrenicectomy after artif. pneu.	None	None	+79° to +83°	+77° to +87°	None	None	Marked increase	No change
GROUP III. CAUTERY LOBECTOMY													
BU		M	Lung abscess	R	Cautery lobectomy after phrenicectomy	None	None	+90° to +95°	+90° to +95°	None	None	Same	No change
GROUP IV. OPEN PNEUMOLYSIS													
WE	37	M	Lung abscess	R	Open pneumolysis c. pneumoth.	To left	More, 2 cm. to left	+94° to +103°	+100° to +144°	None	Improvement	Marked increase	Slight change
WA	21	M	T.B. art. Pneumothorax	R	Pneumolysis	To left	Much more to left	+63° to +69°	+57° to +64°	None	None	Slight increase	Slight change

TABLE I—CONTINUED

GROUP V. EMPYEMA

NAME	AGE	SEX	DIAGNOSIS	SITE	OPERATION	DISPLACEMENT OF HEART SHADOW, BEFORE	SHIFT OF HEART SHADOW, AFTER	RANGE OF ELEC. AXIS, BEFORE	RANGE OF ELEC. AXIS, AFTER	FUNCTIONAL CHANGE	STRUCTURAL CHANGE	RESPIRATORY MOBILITY	ANATOMICAL AXIS
CO	8	F	Empyema	L	Drainage	To right	2 cm. to left	+30° to +37°	+13° to +16°	None	None	Practically none	Moderate
GU	5	M	Empyema	L	Drainage	R	L	+67°	+56° to +68°	T II & III	None	Slight increase	None
AD	3	F	Empyema	R	Drainage	L	R	+69°	+73° to +82°	None	None	Slight increase	Very slight
SI	6	M	Empyema	R	Drainage	L	R	+86° to +95°	+99° to +99°	Dec. Amp. Q.R.S.	None	Slight decrease	None
HO	40	F	Pleurisy LEH.	L	Drainage	R	No change	−4° to −16°	−10° to −20°	None	None	Same	Very slight
GROUP VI. ARTIFICIAL PNEUMOTHORAX													
RA	30	M	Tbc. R	R	1500 c.c. Pneumo.	L	More	+90° to +105°	+103° to +111°	Decreased amplitude	None	Less	Slight change
FR	26	M	Tbc. R	R	650 c.c. Pneumo.	None	None	+13° to −58°	−78° to −83°	None	None	Less	Marked change
BR	64	M	R. middle lobe abscess	R	650 c.c. Pneumo.	None	None	−26° to −50°	−45° to −59°	None	None	Less	Moderate change

do not wish to draw unwarranted conclusions from a single experience, but since this was the only fatality and was a cardiac one, it does suggest that patients showing electrocardiographic evidence of structural change in the heart may be poorer subjects for chest surgery than for other types of operative procedure.

Phrenicectomy.—The aim of this operatoion is to paralyze the diaphragm for the purpose of partially immobilizing and compressing the lower lobes of the lung for such conditions as lung abscess, bronchiectasis, or tuberculosis. The phrenic nerve is exposed in the posterior triangle of the neck where it crosses the scalenus anticus muscle. The nerve is cut and a portion of the distal section is evulsed. The diaphragm on that side becomes paralyzed, assumes a position from one to two and a half inches higher than the other side and remains practically immobile during respiration.

In this group we included four patients. In three the operation was performed on the right side. One showed shifting of the heart shadow, two did not. In one the respiratory mobility of the heart was slightly less, in one slightly more after operation, 5° and 6° respectively. One showed some structural or functional improvement as indicated by the disappearance of notching of R in all leads. This patient previously had a two stage thoracoplasty and is included in that group. It was following the thoracoplasty that the notching of R developed. The disappearance of this abnormality can hardly be attributed to the phrenicotomy. It is more likely due to the time which elapsed between the two operations and the natural recovery processes incident thereto. There was no change in the anatomical axis as indicated by the electrical axis.

The one patient having the left-sided lesion showed a slight shifting of the heart shadow to the right. There was no structural or functional change as indicated by the electrocardiogram. There was slightly lessened respiratory mobility (5°). The electrical axis changed 12° toward left axis deviation, suggesting slight change in the anatomical axis. These last changes may be the result of immobilization of the diaphragm by the operation.

Cautery Lobectomy.—This operation consists in fixing the lung to the chest wall by artificial adhesions if natural ones do not already exist, and thereafter cutting a window in the chest, removing a lobe or a portion of a lobe of lung piecemeal by means of a cautery. The operation in this case was performed for multiple abscesses and bronchiectasis. The fact that the lungs, and therefore the mediastinum, are firmly fixed by adhesions means that the heart is not displaced by the operative procedure. However, we investigated this one case of cautery lobectomy, in which a large amount of pulmonary tissue had been re-

moved to see whether or not a possible change in the size of the pulmonary circulation would give rise to any changes in the electrocardiogram.

The patient showed no change in any of the factors under consideration.*

Open Pneumolysis.—By pneumolysis is meant the cutting of such adhesions as may fix the lung to the chest wall. Both of the two cases included in this investigation had a large cavity in the right lung—one a tuberculous cavity of the right apex, the other a nontuberculous abscess in the middle lobe. In both of these cases bands of adhesions prevented the accomplishment of a collapse of the lung by artificial pneumothorax. The operation consisted of opening the chest cavity, tying the large veins which were found in the adhesions, cutting the adhesions, and then closing the chest tightly. Immediately after the chest wound was closed, artificial pneumothorax was induced and in both instances complete collapse of the right lung was obtained.

In both cases the heart shadow was displaced to the left before operation and considerably more to the left afterward. In one the left border touched the rib shadow after operation. There was no functional or structural change in either. Respiratory mobility was increased in both; in one 33°, in the other 4°. Change in the electrical axis was only 6° each but in opposite directions in the two cases. This suggests very little if any change in the anatomical axis in spite of the marked shift to the left of the heart. Also the inconstancy of the direction of the electrical axis change is of interest.

Empyema With Drainage.—In this group five patients were included. These five patients were treated by the so-called closed method of drainage. Pneumothorax was never present throughout the entire course of treatment. Thus any deviation of the position of the heart from normal before operation was never for an instant increased but steadily diminished from the time drainage was started until the patient was cured. Two patients had right-sided lesions. In both of these the heart shadow was displaced to the left before operation and shifted back to the right afterward. Respiratory mobility was affected in both, showing a decrease of 9° in one and an increase of 9° in the other. One patient showed slight functional change as indicated by decrease in amplitude of QRS in all leads. Neither showed any change in the anatomical axis.

Three patients had left-sided lesions. All showed displacement of the heart shadow to the right before operation and shift of the shadow back to the left afterward. One showed slight increase in respiratory

*Incidentally a few years ago one of us had occasion to remove the entire lower lobe of the left lung, thus leaving the posterior pericardium exposed except for a layer of pleura and granulation tissue. In this case electrocardiograms of the heart were taken by applying the electrodes directly to the pericardium, but no noteworthy findings resulted.

mobility, the other two no change. In one there was slight functional change. T_3 which was inverted became upright, and T_2 increased in amplitude. There was no evidence of structural change. One showed some change in anatomical axis as indicated by a change of 17° in the electrical axis toward left axis deviation.

Artificial Pneumothorax.—The aim of an artificial pneumothorax is to collapse and immobilize one lung. The procedure is applicable in certain cases of unilateral or virtually unilateral pulmonary tuberculosis, bronchiectasis, or lung abscess. The collapse of the lung is obtained by inserting a needle into the pleural space and allowing varying amounts of air to enter.

This group includes three patients, all with right-sided lesions. The heart shadow did not shift in two and shifted slightly to the left in one. There was decreased respiratory mobility in all, varying from 8° to 66°. There was no functional or structural change. In one the electrical axis changed 13° to a frank right axis deviation, in one it changed to a frank left axis deviation, in the other with a left axis deviation to begin with it changed 19° more in the left axis direction. A change in the anatomical axis in all is thereby suggested. The last results are interesting in view of the recent evidence that axis deviation does not necessarily mean preponderant hypertrophy of one or the other ventricle, since the curves showing axis deviation were taken within twenty-four hours after operation and before hypertrophy had chance to take place. They are in accord with what Cohn[2] and others have shown, namely, that the electrical axis is dependent in part on the anatomical axis and the position of the heart in the chest with reference to the lead-off electrodes.

SUMMARY

Of a total of twenty-four observations the relation of shift in the heart shadow to change in the anatomical axis, as indicated by change in the electrical axis, is as follows:

1. Shift with change	11.
2. Shift without change	5.
3. Change without shift	3.
4. No shift and no change	5.

Thus in 66.6 per cent the evidence of change in the anatomical axis coincided with the x-ray findings. The degree, however, was not proportionate. The two cases showing the most marked shift in the heart shadow showed only slight changes in the electrical axis (6° and 4°) practically within the limits of error. One case showing a change of 32° in the electrical axis showed only slight shifting of the heart shadow. Also two cases showing a change of 45° and 91° had no shift of the heart shadow. These results may be interpreted to indicate that the

heart may be considerably displaced as a whole to one side or the other in the chest without changing its anatomical axis, or it may rotate considerably on its anatomical axis without changing its relative position in the chest.

CONCLUSIONS

1. X-ray evidence per se of displacement of the heart is of relatively little importance in determining cardiac embarrassment as compared to electrocardiographic evidence of functional or structural change.

2. Change in the anatomical axis is independent of the direction or extent of displacement as shown by x-ray films and probably depends upon other factors, such as mediastinal adhesions, etc.

3. So far as this series goes, in thoracoplasty there is more cardiac disturbance, from the point of view of the electrocardiogram in operations on the right side than in those upon left.

4. Conduction time was not influenced by the operative procedures in any of the patients of this series.

5. Respiratory mobility may be either increased, decreased, or unaffected, regardless of the side of the lesion and operation. It is most constantly affected by artificial pneumothorax and was markedly decreased in all three patients of this series.

6. Of the operations of this series, that of thoracoplasty seems to put the greatest strain on the heart. This may go hand in hand with the clinical evidence which has indicated the need for multiple stages.

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Department of Clinical Reports

RAPID VENTRICULAR RHYTHM PRODUCED BY PRESSURE OVER THE PRECORDIUM REPORT OF A CASE*

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THE case reported in this paper is that of a rapid ventricular rhythm with A-V conduction normal but with V-A conduction blocked (retrograde block) and a ventricular rate higher than the auricular rate.

CASE REPORT

The patient is a schoolgirl, 13 years old, who had three severe attacks of rheumatic fever with polyarthritis at the ages of 5, 8 and 11 years. She had rheumatic nodules at 11, and a moderate attack of tonsillitis at 10. Heart disease was discovered at the age of 5 during the first attack of rheumatic fever. She had no symptoms until the age of 10 when she began to complain of some dyspnea, palpitation and precordial pain. At present she attends school and is able to meet the ordinary demands of school life. She has never been confined to bed with congestive heart failure.

On October 6, 1927, she was referred to the Adult Cardiac Clinic at Bellevue Hospital. An examination of her heart showed that it was much enlarged, extending to the anterior axillary line. There was considerable precordial heave and tenderness. The first sound at the apex was snappy, the second sound was reduplicated. At the apex there was a localized rumbling diastolic murmur and a harsh blowing systolic murmur, which was transmitted to the left and around the back as far as the right axilla. Roentgen-ray examination showed cardiac enlargement characteristic of mitral disease. The routine electrocardiogram was negative except for sinus arrhythmia. The diagnosis upon admission was rheumatic heart disease (inactive), enlarged heart, mitral stenosis and insufficiency, sinus arrhythmia, class 2A (slight limitation of cardiac functional capacity).

She was seen at the clinic every two weeks and frequently in the ward where special studies were made. Oral temperatures were taken at each visit, and in all instances except four the temperature range was between 99° and 100°, the average being 99.6° F. These temperature readings were checked at different periods during the day and were invariably above normal. As no cause could be found for this consistent elevation of temperature, it was thought that an active rheumatic infection of the heart was probably present. This was also borne out by the fact that precordial tenderness was consistently present. This sign of rheumatic activity has been pointed out by Swift and Hitchcock.[1] Frequent blood counts were taken and found normal except for a relative lymphocytosis. The urine and Wassermann examinations were normal.

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At one of the early routine examinations at the clinic, it was observed that the heart developed a rapid rhythm when pressure was applied upon the chest wall and that when the pressure was released the heart returned to normal. The arrhythmia was elicited at will by thumb pressure and could be maintained without interruption for at least one minute. Through the entire period of observation, from October, 1927, to May, 1929, the method never failed, although recently it has been difficult to elicit the arrhythmia or to maintain it for long stretches. The rapid rate was not attended by any cardiac symptoms except palpitation and some precordial distress, especially when the tachycardia was maintained beyond 10 or 15 seconds. Electrocardiographic tracings identified the rhythm as of ventricular origin.

Just after the application of pressure to the precordium a change of rhythm occurs which persists only while the pressure is applied and immediately returns to normal on the release of pressure. (Fig. 1.) The ventricular rate is faster and the QRS complexes are of lower voltage (this is true also of Leads I and II). The ventricluar rate increases from the normal cycle lengths of 0.56 sec. to varying cycle lengths of 0.44 to 0.36 sec. during the application of pressure. There is no widening of the QRS, and for this reason it is probable that the origin of the ectopic rhythm is above the bifurcation of the bundle. The auricular rate and rhythm remain entirely unchanged, so that during the application of pressure the ventricles are beating at a much faster rate than the auricles. To explain this condition it must be assumed that the rapid impulses from the new ventricular pacemaker fail to reach the auricle and that retrograde block exists. However, there is evidence that conduction from auricles to ventricles is normal. This is shown by the occasional interruption in the ventricular rhythm by normal ventricular complexes, which are probably produced by impulses from the auricle (point C) because the normal P-R interval is present and the ventricular complexes are like those of the normal control. In order to interrupt the ectopic ventricular rhythm, the impulse from the auricle must arrive after the refractory period in the ventricle is over and as a necessary corollary before the ectopic impulse has been initiated. To fit in with this condition a ventricular complex which responds to an auricular impulse must be closer to the preceding ectopic beat than the next expected beat. The ventricular rhythm, however, is so irregular that one cannot anticipate the location of the next ectopic beat. The ventricular complexes resulting from auricular impulses are always very close to the preceding ectopic beat and at no time is that interval equal to 0.44 sec. which is the longest ectopic cycle length.

Only a few cases showing this type of arrhythmia have been reported. White[2] reported such a rhythm in a patient following tonsillectomy and in two others following digitalis. Hewlett[3] has reported similar tracings. In two of White's cases and in Hewlett's case the ventricular rhythm was interrupted by ventricular complexes in response to normal auricular impulses. We have been unable to find in the literature any instance in which the ectopic rhythm described above was produced by

pressure over the precordium. Condorelli[4] applied vigorous percussion in the fifth left interspace to a patient with Stokes-Adams syndrome and was able for a period of two hours to keep up a ventricular rhythm which was identical with the rate of percussion. He later induced ventricular premature contractions by direct percussion in the fifth left interspace in normal subjects. Hoffman,[5] Oppenheimer and Stewart,[6] and Fossier[7] have been able by mechanical or electrical stimulation to induce ventricular premature contractions in patients in whom the heart was covered only by soft tissues.

A study was made to determine whether the rhythm produced was due to a reflex phenomenon or a direct mechanical stimulation of the

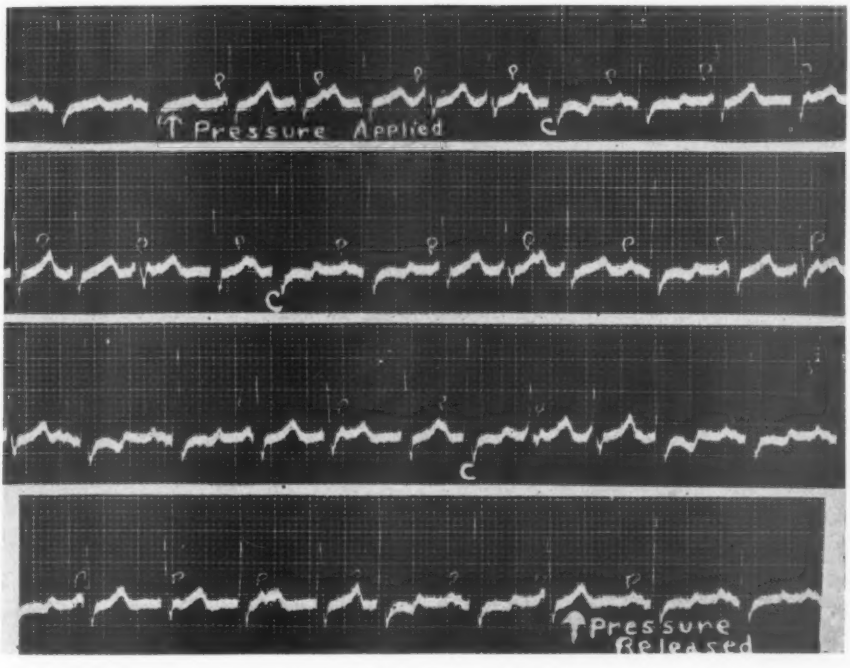

Fig. 1.—The effect of application of pressure to the precordium (Lead II). Tracings are continuous reading from top to bottom.

heart. The skin over the precordium was stimulated in various ways and electrocardiographic tracings were taken. The following methods were used: pinching and twisting, heating with a very hot water bag for twenty minutes, the application of faradic and galvanic currents, and superficial and deep thumb pressure. It was found that deep thumb pressure was the only effective stimulus and that the precordial surface was not uniformly responsive—the most irritable area being located at the third and fourth left intercostal spaces, about one inch from the sternum. Pressure applied within a radius of one inch from that spot would elicit the arrhythmia, but a proportionately greater

force was required as the distance from the center was increased. These observations suggest that the rhythm was not induced reflexly. To rule out any afferent pathway along the intercostal trunks, 2 per cent novocaine was injected to block the intercostal nerves from the anterior axillary line forward. Anesthesia was complete in the third, fourth, fifth and sixth intercostal spaces and partial in the second. Under these conditions deep pressure was quite as effective as before anesthesia. Under the fluoroscope a distinct costocardiac space was seen with the patient in the sagittal plane. When pressure was applied over the anterior chest wall and that space gradually obliterated, the tachycardia could not be induced until the chest wall came in contact with the cardiac shadow. These observations point to an action produced as a result of direct cardiac stimulation. Roentgen-ray and fluoroscopic studies place the most easily responsive precordial spot over a point between the left auricle and the left ventricle.

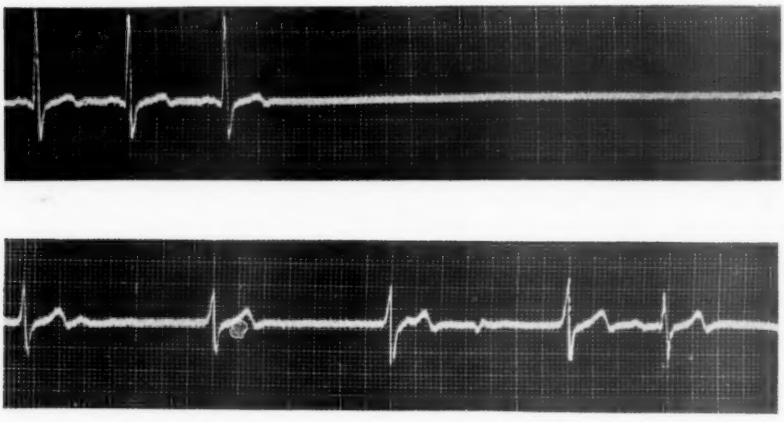

Fig. 2.—Effect of pressure on the eyeball (Lead II). Tracings are continuous reading from top to bottom.

An attempt was made to determine what effect, if any, stimulation or depression of the vagus would have on the arrhythmia, and an effort was made to induce the arrhythmia in other ways than by pressure on the chest wall, such as exercise and the use of drugs—atropine, epinephrin, and digitalis.

Ocular pressure produced a marked bradycardia (Fig. 2), but pressure over the carotid sheath was ineffective. The slowing of the sinus pacemaker was so marked at times that ventricular escape occurred. If pressure over the precordium was applied simultaneously with ocular pressure, the ventricular rhythm was still produced, but with greater difficulty (Fig. 3). This points to some vagal control over the ventricular rhythm. Such a control in ventricular rhythm, particu-

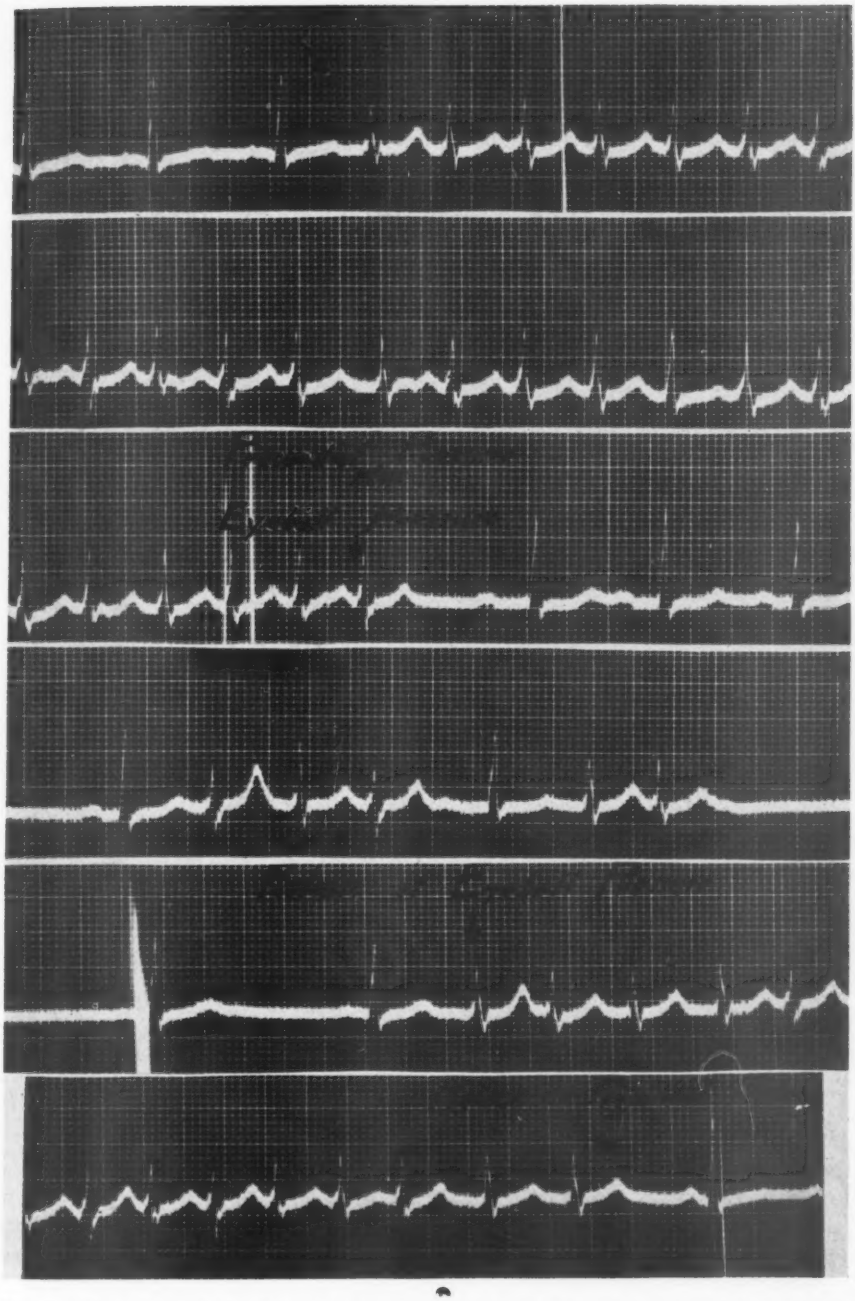

Fig. 3.—The effect of simultaneous pressure on the eyeball and the precordium (Lead II). Tracings are continuous reading from top to bottom.

larly in young patients, has been mentioned previously by Lewis.[8] Hewlett's case[3] shows the same phenomenon.

Since we have evidence that vagus activity may to some extent inhibit the production or maintenance of the ventricular rhythm, it was thought that paralysis of the vagi by atropine might cause the rhythm to be more readily induced. Atropine sulphate (3.0 mg.) was injected subcutaneously. A marked atropine effect occurred, including symptoms pointing to a central action. Sinus arrhythmia disappeared and ocular pressure became ineffective. The heart rate increased from 86 to 109. The rhythm remained of sinus origin, but precordial pressure could initiate the ventricular rhythm more easily than before the administration of atropine.

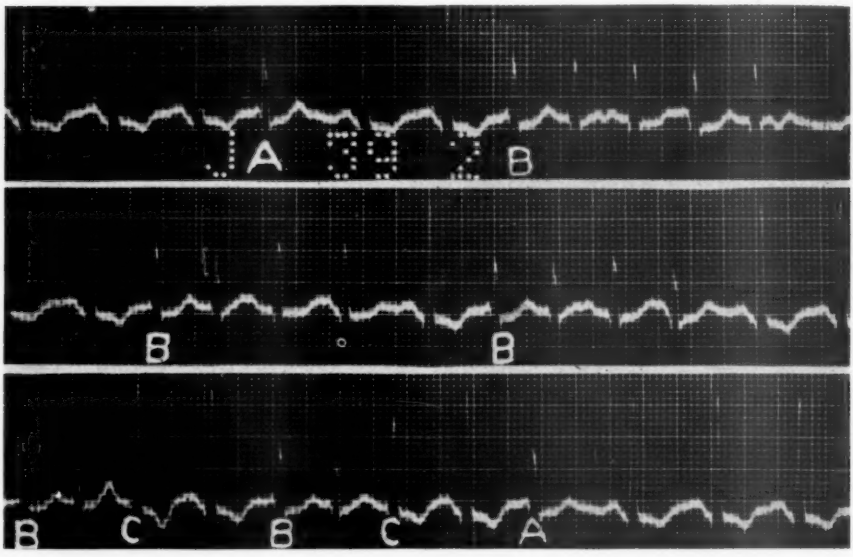

Fig. 4.—Spontaneous origin of the ectopic ventricular rhythm after the administration of atropine and adrenalin (Lead II). Tracings are continuous reading from top to bottom.

The next step was to determine the relationship of the sympathetic to the ectopic rhythm. Epinephrin chloride (1 c.c.) was injected intramuscularly (used in this instance as a sympatheticomimetic). The heart rate increased from 80 to 100 and the sinus rhythm was maintained. Just as with atropine the arrhythmia was produced much more readily than before the administration of the drug. The same observations were made on three different occasions. In order to obtain an epinephrin effect, unattended by vagus action, 3 mg. of atropine sulphate were injected subcutaneously, followed in 45 minutes by 1 c.c. of epinephrin chloride intramuscularly. The heart rate increased from 86 to 140, shortly after the injection of the latter drug. This high rate gradually decreased to 120 per minute at the end of four hours.

Within ten minutes after the injection of the epinephrin the ectopic ventricular rhythm developed spontaneously and thereafter occurred paroxysmally alternating with the sinus tachycardia. The spontaneous paroxysms were short, not exceeding fifteen beats, and in many instances only one ectopic beat would appear. These paroxysms gradually decreased in frequency, the last one observed occurring three and one-half hours after epinephrin was injected, at which time the sinus rate was 130 per minute.

Fig. 4 is an electrocardiogram, Lead II, showing spontaneous origin of the ventricular rhythm. At points *A* the normal sinus rhythm is interrupted by a single ventricular premature contraction, which is definitely premature and is followed by a compensatory pause. At points *B* the normal sinus rhythm is interrupted by runs of ventricular tachycardia. The ventricular premature contractions are exactly of the same type as those of the paroxysms. This, according to Robinson and Herrmann,[9] is suggestive of the ventricular origin of the tachycardia. It will be noted that the P-waves are independent of the ventricular rhythm, due to retrograde block, which is another evidence, according to the same authors, of the ventricular origin of the tachycardia. At points *C* are normal ventricular beats in response to auricular impulses interrupting the ventricular rhythm.

To rule out the possibility that rapid rate alone was responsible for the origin of the arrhythmia, tachycardia with rates exceeding 130 per minute was induced by exercise. The tachycardia so induced was not interrupted by ectopic beats.

The conclusions derived from these observations are that the vagus and sympathetic nerves are both able to influence the arrhythmia. Activity of the vagus prevents the spontaneous origin of the arrhythmias, and its stimulation inhibits the continuance of the ectopic rhythm once it is induced. Stimulation of the sympathetic increases the ease with which the ventricular rhythm is produced, and if at the same time the vagus influence is removed, it initiates the rhythm. The exact part these nerves play in the mechanism could not be determined. It is probable that their action is indirect, in that by decreasing or increasing the irritability of cardiac muscle they render the heart either less or more responsive to impulses emanating from the ectopic focus.

The effect of digitalis was investigated at two different periods, about one year apart. In neither instance was the pressure mechanism affected by the drug. The first investigation was made while the heart was easily responsive to precordial pressure. The patient was digitalized with a single dose of the powdered leaf, using 0.11 cat unit per pound body weight. The electrocardiograms showed many ventricular premature contractions of different origins. In some cases the ventricular premature beats came so early that they began on the T-wave of the preceding ventricular complex. The normal pacemaker was re-

placed by a wandering pacemaker, and there were a few single complexes which resemble those produced by pressure over the precordium. The second set of observations was made at a time when the heart was not readily responsive to precordial pressure. The patient was digitalized very slowly with the same preparation as used before, until there were definite signs of a mild toxicity. Daily electrocardiograms showed no changes except a few premature contractions. We could draw no inferences from these observations with respect to the effect of digitalis on the arrhythmia.

SUMMARY

1. A case is reported in which a rapid ventricular rhythm is produced by pressure over the precordium.

2. The stimulus appears to be a direct pressure effect on the heart, and not a cutaneous reflex phenomenon.

3. The ventricular rate is higher than the auricular rate (ventricular rate 170 per minute, auricular rate 80 per minute). The auricular rate is the same as that before the ventricular rhythm was produced and is in response to the sino-auricular node.

4. Forward conduction is unimpaired as shown by the appearance of normal ventricular complexes in response to the auricular beats which reach the ventricle when it is not refractory.

5. Stimulation of the vagus tends to inhibit the production of the independent ventricular rhythm.

6. Stimulation of the sympathetic when the vagus is paralyzed will induce the arrhythmia.

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ELECTROCARDIOGRAPHIC RECORD OF A PAROXYSMAL CARDIAC IRREGULARITY AS A MANIFESTATION OF THYROID ADMINISTRATION

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THE accompanying electrocardiogram shows a normal cardiac sequence in Leads I, II, and III, with a cardiac rate of approximately 100, until the last cycle illustrated on the third strip of tracing (Lead III). There it will be seen that the auricular rate has increased to 150 with the ventricles following irregularly. On the last strip the auricular rate approximates 400 to the minute, while the ventricular rate throughout this period is quite irregular but as a general rule approximates 150. In places the auricle may be fibrillating. Finally, in the sixth cycle from the end in the last strip the irregularity of the auricle suddenly ceases and the electrocardiogram resumes the picture seen before the attack started. In this transitional cycle there is a hiatus of a complete second between beats of auricle and ventricle; and, when normal mechanism is resumed, the auricle initiates the cycle.

This tracing was made of a patient forty-nine years old who is himself a professor of pharmacology. During the course of a hypertrophic osteoarthritis, it was found that his basal metabolic rate was minus 28 per cent, and he was given thyroid extract for several weeks without any alteration of either the metabolic or the pulse rate. Consequently the thyroid extract was stopped and he was given thyroxin by mouth, 0.8 mg. three times daily. His rate was brought to normal and maintained at normal on this dosage. During the course of this period he developed some edema that seemed most likely to be a manifestation of cardiac insufficiency, and he received tincture of digitalis, 3 c.c., daily until the edema disappeared and alterations were noted in the T-wave of his electrocardiogram.

Three weeks before this tracing was made it was noticed that the P-R time had increased to 0.20 second. Digitalis was discontinued and was not resumed again in the interval prior to the attack of paroxysmal cardiac irregularity which is depicted. While he was on digitalis, his vital capacity rose from 3171 to 3845 c.c. At this time his basal metabolic rate was plus 4 per cent, and he was taking 2.2 mg. of thyroxin daily. Two weeks before the attack noted his basal rate and vital capacity were again measured and were unchanged. On the day on which the tracing was made he had come for estimation of his basal rate, and it was found to be minus 3 per cent with a vital capacity of 4146 c.c. While he was dressing, his heart became a little

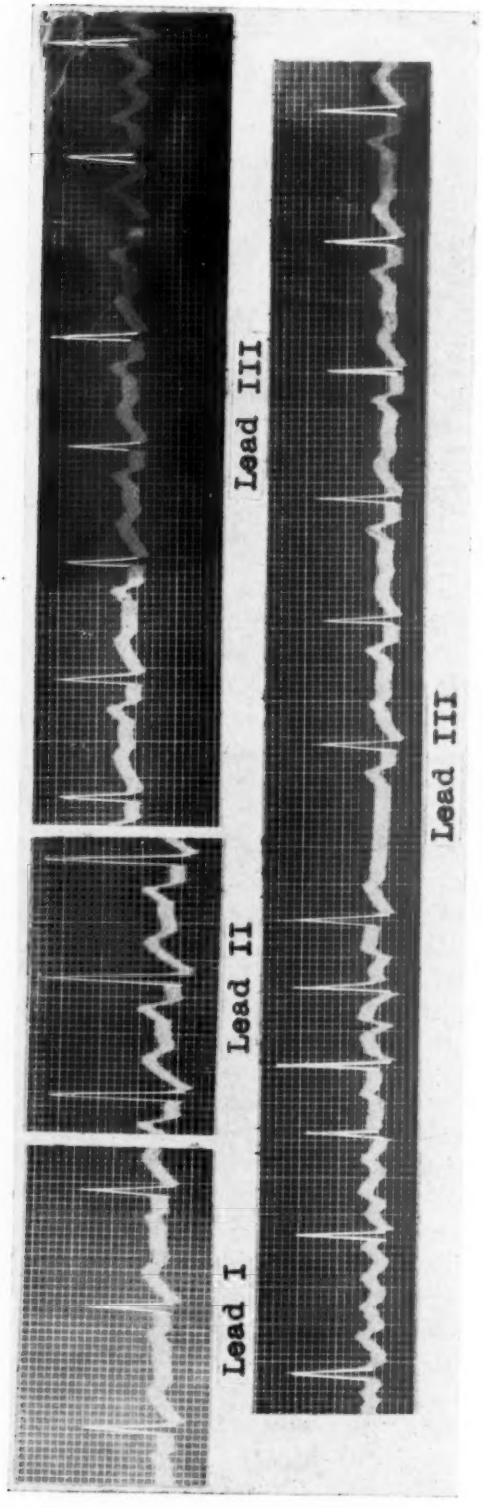

Fig. 1.

irregular and it was in that way that the accompanying tracing was obtained. The attack of irregularity lasted for two minutes; a complete record was obtained, but only the beginning and the end are shown here. He had had no digitalis for three weeks; and, though he was taking thyroxin, he had not taken a sufficient amount to elevate his basal metabolic rate above normal. As a result of this attack, the thyroxin was stopped for almost a month during which time he experienced no further cardiac attacks and his basal rate slipped back to plus 29 per cent with a basal pulse of 64.

The paroxysmal cardiac irregularity picture apparently occurred as a result of thyroxin administration, even though a sufficient amount was not given to raise the basal metabolic rate above the normal. The tracing itself is of importance in that it depicts (1) the transitional cycles between normal mechanism and the beginning of the irregularity and (2) the end of the irregularity and the resumption of the normal cycle.

Department of Reviews and Abstracts

Selected Abstracts

Morawitz, P.: Prevention of Sudden Deaths From Heart Disease. München. Med. Wchnschr. **76:** 1075, 1929.

The author believes that in many cases it is possible to recognize disturbances in cardiac function which are very likely to lead to ventricular fibrillation and sudden death. Suggestive symptoms include anginal attacks, especially during rest, cardiac asthma, attacks of tachycardia, weakening of the apex impulse and a fall in a previously high blood pressure. Electrocardiographic changes include lengthening of the P-Q and Q-R-S intervals with arborization block, absolute arrhythmia, the Pardee wave and negative T-wave.

Believing that quinidine would be of value in preventing the onset of ventricular fibrillation, the author began in 1928 to give it routinely in all cases where he suspected this possibility. His results of 1928 are compared with control data in 1927.

	CONTROL 1927	QUINIDINE 1928
Sudden deaths	43	19
Compensated	24	5
Decompensated	19	14

He concludes that quinidine is of great value in preventing sudden deaths, especially in compensated arteriosclerotic and luetic cases, where the cardiac damage is not particularly extensive. He gives it for long periods of time in doses of 0.2 gm. daily and has observed no ill effects.

Fischer, Robert, and Kiss, Aristed: A Contribution to the Knowledge of Pararrhythmia. Deutsche Arch. f. klin. Med. **164:** 73, 1929.

A case is presented of nodal rhythm alternating with cycles of normal sinus rhythm and occasional auricular extrasystoles. The cycles of normal rhythm always appeared after a definite interval following the previous nodal systole; and the successive cycles showed an increase in time interval, although at the same time there was a decrease in conduction time. The explanation for this increase in time interval is not quite clear.

Haag, Harvey B., and Hatcher, Robert A.: The Stability of Digitalis and Its Preparations. J. A. M. A. **93:** 26, 1929.

Six specimens of powdered digitalis have been examined after intervals varying from one to sixteen years, and in no case has deterioration been detected, and the authors believe that no one working in their laboratory has ever observed anything indicative of deterioration in one of the many specimens of powdered digitalis used. Powdered digitalis in capsules or in tablets is admirably suited for securing uniformity of doses where individual patients, clinics or groups of clinics are provided with sufficient amounts to last one year or more.

A sterile infusion of digitalis undergoes little change within several months, and deterioration then results solely in diminished activity, not in increased toxicity.

The offical tincture of digitalis retains its activity with comparatively little change during the several years, and any change that does occur merely calls for a corresponding increase in dosage. The secret of deterioration of liquid preparations has not been explained fully, and there is no evidence that any of these preparations are as stable as powdered digitalis kept with ordinary care in a corked glass bottle.

Aqueous solutions of strophanthin, ouabain or other digitalis principles, kept in ampules of soft glass deteriorate rapidly. Ouabain solution in ampules of hard glass decompose slowly. There is no evidence that any of the digitalis specialties in use are more stable than the official digitalis tincture.

Schwartz, Sidney P. and Weiss, Morris M.: Digitalis Studies on Children With Heart Disease. The Effects of Digitalis on the Electrocardiograms of Children With Rheumatic Fever and Chronic Valvular Heart Disease. Am. J. Dis. Child. **38**: 699, 1929.

A summary of the results obtained from the administration of a single body-weight dose of digitalis to 24 children with chronic rheumatic valvular heart disease and signs of heart failure reveals that the use of the drug by this method is a safe procedure in children exhibiting sinus rhythm or an irregular ventricular rate due to auricular fibrillation. There were no untoward symptoms from the administration of the drug in a single dose of this type provided it was well diluted with water.

The changes induced by the drug were recorded in 12 of 18 children with sinus rhythm and in 5 children with auricular fibrillation who were studied during both the active and inactive phases of rheumatic fever. The alterations produced on the electrocardiogram consist essentially of a lowering of the S-T segments below the isoelectric line with final progressive increases in the negativity of the T-wave in one or more of the leads in which it was previously upright. In 2 children a previously negative T-wave in Lead III eventually became positive. In 6 of the eighteen children no electrocardiographic signs of digitalis action were observed.

A transitory slowing of the sinus rate of between 10 and 15 beats per minute in 12 children with sinus rhythm and a reduction of the ventricular rate in auricular fibrillation from an average of 157 beats per minute to 60 beats per minute within twenty-four hours was observed following the dose of digitalis. In one child the administration of digitalis augmented the size of the P-R interval during an attack of rheumatic fever.

The inconstancy and variability of the appearance and duration of the changes induced by body-weight doses of digitalis on the S-T interval and T-waves of the electrocardiograms of children make this method of studying the doses of digitalis in children totally inadequate. For similar reasons, the effects of digitalis on the electrocardiograms of children cannot be taken as criteria in measuring the standardization of the drug, its rate of absorption and elimination or the daily amount necessary to maintain its persistent effects known as the maintenance dose.

Cloetta, Max: The Biochemical Action of Digitalis. J. A. M. A. **91**: 1463, 1929.

The author in this article discusses briefly his conclusions as to the action of digitalis preparations on the heart muscle from a pharmacological standpoint. He presents certain conclusions that are of a clinical nature. He believes that digitoxin has a more important and a more lasting effect on the heart muscle than any of the other derivatives from folia digitalis. From a study of the mechanism of cardiac response, he believes that under the influence of digitalis the cardiac muscle is

capable of overcoming a greater resistance without having to undergo dilatation. In studying animals with experimental valvular lesions of the heart, he has found that if digitalis is administered to these animals immediately after the aortic defect develops and the treatment is regularly continued, then the dilatation and hypertrophy never reach the high degree attained without digitalis treatment. When these aortic deficient hearts are compared with normal hearts as to their absolute reserve energy, one finds that the crippled digitalis-treated heart is almost equal to a normal one while the defective heart without digitalis treatment is much more rapidly exhausted. He believes that this should be sufficient to induce prophylactic treatment with digitalis in all early cases of endocarditis which are apt to terminate in valvular lesions.

A further discussion of the mechanism of digitalis action is presented. The author believes that digitalis has both fixed and reversible actions on the heart muscle, that is, certain derivatives, particularly digitoxin, become fixed in the heart muscle cells in such a way that it cannot be released by any physical process.

The relationship of calcium and calcium therapy to digitalis is fully discussed.

Harvey, E. Newton: The Effect of High Frequency Sound Waves on Heart Muscle and Other Irritable Tissues. Am. J. Physiol. **91:** 284, 1929.

High frequency sound waves of high intensity will cause rhythmic contraction of quiescent ventricular muscle of frog or turtle immersed in Ringer's solution and a more rapid natural rhythm of the auricles accompanied by lessened amplitude of contraction and often by increased tone. Touching ventricle or skeletal muscle or nerve to glass carrying intense supersound waves does not stimulate, but nerves and skeletal muscle of frog or turtle containing nerves show a few subminimal twitchings of short duration when immersed in Ringer's solution. The effect may be due to increased pressure changes accompanying the sound waves, since it is known that increased pressure will stimulate.

Schneider, Edward C., and Ring, Gordon C.: The Influence of a Moderate Amount of Physical Training on the Respiratory Exchange and Breathing During Physical Exercise. Am. J. Physiol. **91:** 103, 1929.

Following a study of the effects of moderate physical training on the basal respiratory exchange, pulse frequency, and arterial blood pressure, the authors have studied the changes in the position of the "crest-load" in the respiratory exchange and in the minute volume of breathing for two subjects while performing physical work through a period of regular physical training and during an after period when no exercise was taken in order to determine how soon and to what extent moderate regular exercise may influence each.

The percentage of carbon dioxide in the expired air of a work period has been used to determine the amount of work that constitutes a "crest-load"; so long as the percentage of the exhaled carbon dioxide rises proportionately with added increments of work the load is considered normal. The crest-load is reached when the oxygen-supplying mechanisms working at full capacity just meet the oxygen need of the reconversion process of the muscles. With this load the percentage of exhaled carbon dioxide is at its maximum. A further increase in the load of work becomes an overload and is associated with the escape of lactic acid from the muscles into the blood and a proportionate reduction in the formation of carbon dioxide. When this occurs, the percentage of carbon dioxide in the exhaled air is less than it is with the crest-load.

Moderate physical training, about an hour daily, increased the load-carrying ability within one week in the subjects studied, but the full effects were only ob-

served after five to seven weeks. Any let-down in the regularity or amount of daily work soon reduced the load-carrying ability, but even with complete neglect of exercise some of the gain in power was maintained for several months. The percentage of carbon dioxide exhaled and of oxygen absorbed during work is increased by training, the full effects being reached within four or five weeks. These soon drop back to the pretraining level when training is discontinued.

The minute volume of breathing for any given load of work decreases with training and reaches its lowest level in from four to six weeks. This effect disappears within four to six weeks after training changed overloads to normal or crest-loads. In one subject the absorption of oxygen was increased as training changed overloads to normal or crest-loads. In another subject a slight decrease in the oxygen consumption of work was evidenced as training proceeded. A decrease in the respiratory quotient of work during training suggests a gain in ability to reconvert lactic acid more adequately into its precursor.

Simpson, R. H., and Batten, Lindsey W.: Some Points in the Diagnosis of Cardiac Lesions in Children. Lancet 2: 372, 1929.

An attempt has been made to indicate the main differences between child and adult cardiology and to point out some of the problems peculiar to children and how they may be faced.

The diagnosis of fully developed lesions is on the whole easier in children than in adults and even prognosis is in some respects less difficult than it becomes after middle life but the problem of the early developing lesion is at times one of the greatest difficulties. To form an opinion on the state of the heart at the moment of examination may not be hard, but there will arise the question "is this heart the seat of active infection—is this slight abnormality the first sign of serious trouble?" To answer this question a thorough and general investigation of the child and his history will be necessary, and in some cases a period of observation while the diagnosis remains in doubt cannot be avoided. Such cases are, however, the exception and not the rule. In very many cases brought up for decision the diagnosis of "healthy heart in a healthy child" can be made with confidence. In another group, the nature and degree of cardiac damage can be stated with reasonable certainty, the present infection excluded, a suitable regimen instituted and a watch kept for any recurrence of active trouble. In doubtful cases the necessity for reaching a decision at the earliest possible moment should never be forgotten.

The insidious nature of the rheumatic infection and the variation of its manifestations has lately been emphasized. Parents, teachers and others responsible for the health of children should take early and serious notice of fidgetiness and joint pains, fever and tonsillitis. The doctor knowing well the damage rheumatic infection can do is tempted to an attitude of extreme caution. This is from one point of view amply justifiable. It must be remembered that while childhood is the time when rheumatic infection does its worst, it is also the time when accidental and insignificant murmurs are commonest and the pulse rate most variable and easily disturbed, and furthermore, it is the time when character and emotional outlook are being formed. Six months of rest in bed to recover from cardiac dilatation may prove to be invested soundly: six months of doubt and caution with restrictions of play and exercise in an atmosphere of anxiety are unlikely to stay the progress of an insidious carditis but are well calculated to sow the seeds of a cardiac neurosis difficult or impossible to eradicate.

Hooker, D. R.: On the Recovery of the Heart in Electric Shock. Am. J. Physiol. **91**: 305, 1929.

A new method based on physiological principles for the recovery of the heart in electric shock is described, and the results from its use are reported. This method although complicated and difficult of practical application seems, as judged from the results obtained, to promise a real advance in control of ventricular fibrillation.

Ventricular fibrillation is believed to be the most common cause of death in electric accidents. In the dog, as is assumed to be the case in man, ventricular fibrillation when once established is all but invariably permanent with resultant death, since the fibrillating ventricles are incompetent to maintain the circulation.

Potassium chloride is the only agent of demonstrated efficacy in overcoming ventricular fibrillation. It acts by producing a state of inhibition. This inhibition, in turn, can be overcome by removing the excess potassium from the coronary vascular bed.

With these facts in mind, experimentation led to a procedure suitable for the resuscitation of dogs in which ventricular fibrillation had been induced by electric shock. This procedure calls for the central carotid injection of the remedial solutions, saturated with oxygen and warmed to body temperature. The first solution of potassium chloride 0.5 per cent, sodium chloride 0.9 per cent, and heparin 0.25 mg. per c.c. establishes potassium inhibition, and the heart is allowed to rest for one minute. The second solution, calcium chloride 0.025 per cent and sodium chloride 0.9 per cent, washes the excess of potassium out of the coronary bed and substitutes a relative excess of calcium chloride, the effect of which is to stimulate a normal cardiac rhythm. This effect is enhanced by the coincident injection of 1 c.c. of 1:1000 adrenalin chloride.

The author states that such an approach to the problem of resuscitation from ventricular fibrillation has not heretofore been suggested and it has resulted in a number of spectacular recoveries. The method should, however, be subjected to further critical study before considering its application to man because there are obvious indications that it may be improved, particularly for use in cases of long-lasting fibrillation.

Veil, W. H.: Rheumatic Infections. Deutsche Med. Wchnschr. **55**: 556, 1929.

The author holds that rheumatic fever may primarily involve the renal glomeruli, causing an acute or chronic glomerulonephritis. The subsequent development of typical migrating arthritis or of endocarditis gives a clue to the renal picture. In two cases with uremic manifestations, very marked improvement occurred following tonsillectomy.

Not only the renal glomeruli but the renal capsule likewise may bear the brunt of a rheumatic infection. The author uses the term perirenitis; and cites a very interesting case. This was a patient forty-five years old, with rheumatic pericarditis and a diminished urinary output, who had been under treatment with salyrgan and strophanthin for the relief of edema. A tumor the size of a child's head was found in the position of the right kidney, and a markedly diminished secretion was obtained from this kidney on ureteral catheterization. At the exploratory operation there was found a large spongy sac consisting of loose connective tissue in the depths of which a small discolored kidney was embedded. After splitting the kidney capsule proper, the kidney immediately assumed its normal size and color. Directly thereafter, the urinary output became normal.

Graham, Evarts A.: Decompression of the Heart. Ann. Surg. **90**: 817, 1929.

The purpose of the paper is to record two cases in which operation was performed for the deliberate purpose of decompressing the heart. The principle of this decompression is likened to that of decompressing the brain or thorax when there is present increased pressure within the cavity. The author discusses the question of the heart that may be embarrassed by confinement within a bony chest wall apart from whatever embarrassment may result from restriction of its movements by pericardial adhesions. In the two cases reported, the pericardium was not thickened and in the second case, no adherent pericarditis was present. Both cases had suffered from periods of cardiac decompensation and embarrassment and showed a very marked enlargement of the heart. Following thoracoplasty over the precordium, both patients obtained marked subject improvement. In the second case there was objective disappearance of a raised venous pressure and nodal rhythm which had been present before. Both patients lived several months after the operation in comfort until they died, the first of an acute pulmonary infarct, and the second of acute pneumonia.

Dickson, D. Elliot, and Dickson, W. Arnott: Arteriosclerosis in Coal Miners. Brit. M. J. **2**: 1103, 1929.

The results of a consecutive examination of the circulatory system of 500 coal miners are studied. It is shown that among coal miners of all ages there is an extraordinary prevalence of thickened arteries; the thickening is confined to the intima in the specimens examined. There is no associated rise in blood pressure. There is an unexplained difference in the mortality rate of coal miners as compared with other males.

Of the 500 individuals examined, 116 were twenty years or under, 180 were twenty-one to thirty years; 111, thirty-one to forty years; 61, forty-one to fifty years; 32 were over fifty years of age. Of 500 miners examined only 44 had arteries which could not be palpated. These occurred principally among those individuals under thirty years of age. Two individuals, both of whom were over fifty years of age, had arteries so thickened as to be classified as atheromatous. These showed marked calcareous degeneration. After the age of forty years, none of the men had arteries which were not palpable. Four hundred forty-nine cases out of 500 had blood pressure falling within normal limits, and only 51 showed blood pressure over 140. It is suggested that the arteriosclerosis shown to exist in coal miners is the explanation of the peculiarity in their mortality rate. In an attempt to explain the reason for this arteriosclerosis, the authors have found that the only significant constant factors are: (a) the inhalation of air of altered composition, especially the CO_2 content; and (b) the absence of daylight.

Robertson, H. F.: Vascularization of the Thoracic Aorta. Arch. Path. **8**: 881, 1929.

Following the suggestion of Klotz that the localization of syphilitic lesions in the ascending aorta might have an anatomic basis, the author has studied the vascularization of the thoracic aorta. The hearts of dogs, lambs and human beings were injected by aortic cannulas so that the first coronary branches which gave vessels to the aorta were always filled. Radiography, dissection of cleared and uncleared specimens, and corrosion of specimens were carried out. Serial sections gave the details of the distribution of the vasa vasorum and other fine vessels.

From the data furnished by these experiments, the thoracic aorta may be roughly described as vascularized by a sheath of areolar connective tissue richly supplied with blood vessels. Over the arch and the descending thoracic limb, this sheath

contained at least two distinct layers of interweaving vessels which were derived from vessels of adjacent structures or from branches of the aortic efferent vessels. Over the ascending limb, only a single network was usually seen, derived from coronary branches from cardiac fat-pad branches of these and from descending vessels of the aortic arch. At the root of the aorta, the richest vascular bed was found.

The author believes that the blood vessels are found to be most numerous in the aortic wall where aortic disease other than senile change is the most commonly localized. A relation exists between the presence of certain lesions of the aortic wall and the distribution of the vasa vasorum.

Semsroth, Kurt, and Koch, Robert: Studies on the Pathogenesis of Bacterial Endocarditis. Arch. Path. 8: 921, 1929.

In human endocarditis, the earliest endocardial change has until recently generally been supposed to be an "endothelial damage" preceding the localization of bacteria. This endothelial damage has never, however, actually been observed. Mononuclear endocardial cell proliferation, on the other hand, is a well-known constituent of human endocarditis. Autopsies on several patients who showed early endocarditis showed the authors the possibility of studying early endocardial reactions in endocarditis. In these patients nodular monocytic proliferations were not infrequently observed underneath an intact endothelium and far from the site of thrombotic deposits. This observation allows the conclusion that monocytic endocardial proliferations in human endocarditis are not invariably the sequel of thrombotic deposits. Furthermore, in several mononuclear endocardial cell proliferations, areas of transformation of the intercellular substance into hyalin were found associated with a defect of the surface endothelium but without a thrombotic deposit. The authors infer that these cellular proliferations may arise in the absence of thrombotic deposits and may through regressive changes develop endocardial defects which in turn may become the site of thrombi.

In other words, nodular mononuclear cell proliferations of the human endocardium may precede the formation of morphologically detectable endocardial defects and endocardial thrombotic deposits.

In studying the reactions of animals to protein sensitization for other purposes, the authors have noted similar nodular mononuclear cell proliferations; and they, therefore, raise the question as to whether or not these processes may not be somewhat related to the sensitization processes of human rheumatic fever. This inference that bacterial localization on the endocardium results from its altered capacity to react toward bacteria would seem logical. This relationship, however, is scarcely true within the confines of specificity as the "allergic state," so-called may be induced by a nonbacterial foreign protein.

Ceelen, W.: Present Status of Myocardial Lesions. Deutsche med. Wchnschr. 55: 569, 1929.

The author briefly discussed the common pathological lesions of the myocardium. He calls attention to a peculiar type of myocarditis occurring in children in the first two years of life, often associated with status lymphaticus. The following case is cited as an example: A child, five months old and previously well, became ill suddenly and died within twenty-four hours. The ventricles of the heart were enlarged, and an extensive lymphocytic infiltration was found in the myocardium, causing considerable destruction of the muscle fibers. Although this lymphocytic infiltration might be considered as the accompaniment of a status lymphaticus, the author favors an infectious origin.

Fahr, Th.: Cystic Kidneys as a Cause of Constant Hypertension. Deutsche med. Wchnschr. 55: 572, 1929.

The author believes that cystic kidneys can cause cardiac hypertrophy and hypertension only which the kidney parenchyma is seriously involved.

Dietlen, H.: Problems in the Pathology of the Circulation. Deutsche med. Wchnschr. 55: 566, 1929.

The question is raised whether in certain disturbances of the circulation the capillary function may not be primarily involved, with secondary cardiac embarrassment. The rôle of the capillaries in the control of the return circulation to the heart is evident from: 1. The ability of the spleen and the subpapillary dermal plexuses to act as reservoirs of large quantities of blood, said at least to be one liter. 2. Variations in the size of the capillary vessels as a result of changes in the hydrogen-ion concentration of the surrounding tissues.

The author suggests that one should look for capillary disturbances in cases refractory to digitalis.

Lundy, Clayton J., and Woodruff, Lewis H.: Experimental Left and Right Axis Deviation. Arch. Int. Med. 44: 893, 1929.

Using a method previously described by the authors of placing and distending a balloon in various chambers of the heart and in the great vessels, electrocardiographic evidence of right and left axis deviation was studied. The method permits electrocardiographic observation of the effect of increased pressure within and distention of the cardiac cavities and of obstruction to blood flow in the great vessels of the intact young dog under light ether anesthesia. Several undesirable features of the method of study are discussed in this paper. The desirable features are that the method may be used on the intact dog, that complete recovery occurs enabling one to repeat the experiments many times on the same dog. It is also possible to influence separately either the right or the left ventricle.

Acute dilation of the right ventricle was produced with corresponding right axis deviation. The authors then discuss the possible factors in these experiments for the production of axis deviation and various arrhythmias of the heart. They state that stretching of the muscle cells of the individual ventricles produced directly by the balloon or distention with blood may cause increased permeability of the cell membranes, thereby increasing the excitability of that individual ventricle with corresponding electrocardiographic evidence of axis deviation. They also believe that the lowered resistance produced in this manner between the individual cells may account for a small part of the axis deviation. Another explanation may be that partial asphyxia may cause an increased permeability of the cell membranes or may change the character or concentration of the electrolytes contained within the cells making them more diffusible.

Other possible explanations are: (1) The rate of propagation of the action current may be increased; (2) there may be a change in the direction of the action current associated with a change in the direction of the nerve fibers caused by distention with the balloon; (3) there may be a change in the relative volume or mass ratio between the left and the right ventricles; (4) factors of decreased as well as increased excitability may be present. The possible importance of these and similarly acting factors as a mechanism for clinical changes of the electrocardiogram is discussed.

Hartman, Howard R., and Ghrist, David G.: Blood Pressure and Weight. Arch. Int. Med. 44: 877, 1929.

This study has been undertaken for the purpose of determining the relationship, if any, that exists between arterial blood pressure and body weight. To obtain the data for this study records of 2,042 consecutive registrants fifteen years old or more were taken from the files of The Mayo Clinic for June, 1927. Nine hundred and fifty-nine of the subjects were males and 1083 females. By use of the Nylic standard table of heights and weights, percentage deviation from normal weight was computed in each case. The arrangement of groups by percentage deviation from normal was then accomplished for males and females.

In the charts there is shown in males an almost step-like rise from the group 26 to 50 per cent underweight to the group 51 to 75 per cent overweight in the mean values for the systolic blood pressures of the groups. The most significant rise of systolic blood pressure is demonstrable between normal weight and 11 to 25 per cent overweight. The marked difference between the total underweight and the total overweight male groups is strikingly significant. In the female group there is a similar step-like rise in the systolic blood pressure. The marked difference between total underweight and total overweight between groups is practically as striking and is equally as significant as it is in the males.

Hartman, Howard R., and Brown, George E.: The Systolic Blood Pressure in Duodenal and in Gastric Ulcer. Arch. Int. Med. 44: 843, 1929.

This study was undertaken to determine whether or not patients suffering from duodenal or gastric ulcer have low systolic blood pressures. The data were compiled from the records of patients with duodenal or gastric ulcer examined in The Mayo Clinic by a diversified group of internists. Thus multiple personal equations are expressed in the readings which were taken without the subject under consideration in mind. The readings were recorded immediately on a history sheet, and from these records the charts were compiled and curves constructed by a statistician, who had no knowledge of the preconceived hypothesis. The calculations and mathematics of biometry were checked throughout by other statisticians. The first series of cases studied comprises 865 of duodenal ulcer and 561 of gastric ulcer. In selecting the patients, the question of whether blood pressure was normal or abnormal was not considered. The series included cases of severe hypertension due to independent conditions associated only by coincidence. The data were corrected for age and weight against 1016 cases encountered in the routine of work at the clinic.

In order to make the comparison fairer, three additional groups were studied. One of these comprised 1,685 cases of cholecystitis. In 782 cases in this group cholelithiasis was present. The second of the three additional groups to undergo analysis was made up of 571 cases of inoperable carcinoma of the stomach and 239 cases of carcinomatous gastric ulcer. The third additional group was made up of cases, the reports of which were obtained from one life insurance company. The "normal blood pressure curve" that was used by the company was not included, but derived averages of calculation from the frequency distribution of the various blood pressures in five-year age groups of all persons who applied for life insurance during a given period were taken as the curve for comparing with the other groups.

The blood pressures in cases of duodenal and gastric ulcer compared with the curve constructed from life insurance statistics are lower in men and in the sexes combined, but are not lower in the females alone. Too much stress, however, cannot be placed in this comparison because of the fact that the insurance cases were not corrected for weight and the other groups were not corrected against a

normal blood pressure but against a control group. The blood pressures in this control group also are higher than those in the ulcer group in both males and females, but the variation is not of significance. The curves remain fairly parallel throughout all ages.

In comparing the blood pressure in cases of duodenal and gastric ulcer with that in cases of cholecystitis and carcinoma of the stomach or carcinomatous ulcer, the difference is not significant in either males or females.

Major, S. G.: Blood Pressure in Diabetes Mellitus. Arch. Int. Med. 44: 797, 1929.

Blood pressure in a clinical series of 500 cases of diabetes mellitus is compared with the blood pressure in three control groups. The first control group consisted of 356 dispensary patients, all of whom were thirty-five years or older. In the second control series, the blood pressures in 472 consecutive hospital cases were studied. These cases as well as those in the former group were taken regardless of the complaint of the patient. In the third control series blood pressures were taken on apparently normal persons. In the 500 clinical cases of diabetes mellitus, 408 were thirty-five years or older. The figures obtained from the study are subjected to a statistical analysis.

In elderly diabetic patients, systolic blood pressure is slightly higher than that of patients seen in a dispensary series or in a hospital series and considerably higher than the blood pressure in normal persons of the same age group. Although the mean systolic blood pressure in the diabetic series is not essentially different from that in either the dispensary series or the hospital series, there is a greater tendency to a slight elevation of the systolic blood pressure in diabetic persons than in those in the other series mentioned, as is shown by a statistical study.

In a study of 104 cases of diabetes mellitus coming to post-mortem examination, all cases showing vascular injury were excluded. In the remainder, after calculating the mean weight, according to sex and also according to five-year age groups, it was found that the weight of the heart of the men in the diabetes series exceeded that of the men in the control series after the fifty to fifty-five years of age group; whereas the weight of the heart of the women in the diabetic series exceeded that of the women in the control series after the age of sixty-five to seventy years. When both sexes were included in this comparison, it was found that the curve representing the diabetic series was higher than that representing the control series after the age of fifty to fifty-five years. It was found that the kidneys in the diabetic series weighed slightly more than those in the control series.

Pardee, Harold E. B.: Experiences in the Management of Pregnancy Complicated by Heart Disease. New York State J. Med. **29**: 267, 1929.

Whether or not to allow a woman with heart disease to go through pregnancy depends on a prognosis. This prognosis depends upon the functional cardiac diagnosis, and this depends upon the patient's ability to perform physical exertion rather than upon the pathological state of the valves or myocardium. MacKenzie pointed the way to a better understanding of the problem by focusing attention upon the symptoms and signs of failure of the heart to maintain a normal circulation rather than on a diagnosis of an anatomical lesion. This report is based on the results in 106 patients in the antepartum clinic of the Lying-In Hospital, New York, from July, 1923, to July, 1925. Two of the patients had congenital cardiac abnormalities, one a patent ductus arteriosis. The others all had rheumatic heart disease. Mitral insufficiency was diagnosed in 29 patients; mitral stenosis in 64 and aortic insufficiency in 11, 3 of whom had also some degree of mitral stenosis. The patients

were classified according to the nomenclature adopted by the New York and American Heart Association. In Class I, there were 75 patients; in Class IIa there were 20, and in Class IIb there were 11. Six other patients admitted to the hospital during labor with heart disease in a seriously decompensated state belonged to Class III. Three of these patients showed pulmonary edema. The author believes that this functional classification serves as the best means for handling women during pregnancy. He believes that cardiac enlargement is not a reliable guide, since several patients showed marked degrees of enlargement without signs of compensation during labor. The prognosis will depend a great deal on the type of labor that ensues. When this is short in the first and second stages, the outcome will be favorable. He believes that the obstetrician should determine in each instance what measure should be adopted to hurry up safely the duration of labor.

In the antepartum clinic, the best treatment of these patients is the prevention of severe cardiac failure, and this means keeping watch during pregnancy for the appearance of increasing cardiac difficulty, appropriate treatment of the heart as soon as this is discovered, and interruption of pregnancy if the heart fails to respond to treatment after two or three weeks. In these patients cesarean section was performed on several occasions and seemed to produce very little strain on the heart. The results are better than from hysterectomy. Gas anesthesia during labor or during operation should be avoided, since it produces cyanosis and increased strain on the heart. Ether or chloroform were well tolerated. In this series of patients deaths occurred only in Class IIb and III. One patient in Class IIa died of pneumonia after operation, but there was no apparent effect from the heart.

The author concludes that Class I patients will not be in trouble during pregnancy or delivery under proper care, that Class IIa will probably not give trouble, that Class IIb will probably give trouble, and that Class III is a very difficult group to handle safely and that in this group the mortality is very high.

Levine, Samuel A., and Walker, George L.: Further Observations on Latent Hyperthyroidism Masked as Heart Disease. New Eng. J. Med. **201:** 1021, 1929.

Attention is drawn to a group of patients usually treated for heart disease in whom the underlying cause is a latent and unrecognized hyperthyroidism. These cases are generally overlooked, for the common signs and symptoms, exophthalmos and thyroid enlargement, usually found in typical exophthalmic goiter and toxic adenoma are not evident in these patients. The diagnosis is even more difficult in patients who have coexisting organic heart disease such as angina pectoris, hypertensive heart disease or mitral stenosis. Of special interest are those with typical anginal attacks in whom proper treatment of the latent hyperthyroidism results in a great reduction in the number of attacks if not complete relief from symptoms.

The diagnostic criteria are discussed, and attention is especially directed to certain points in the general appearance of the patient, and in the physical findings which lead one to suspect the presence of a latent hyperthyroidism. These minor features are: periods of inexplicable diarrhea, unexplained loss of weight, nervousness, tremor, sweating and a feeling of warmth. Palpitation, shortness of breath, precordial pain and muscular weakness are of course common complaints, but they occur just as well in heart disease without as with hyperthyroidism, and therefore are not particularly distinctive.

Circulatory insufficiency is not a contraindication for surgery in the treatment of these patients, many of whom are relieved completely and others much improved by subtotal thyroidectomy.

A series of eleven cases is reported, all of which had been treated for a considerable period of time for heart disease, but in each of which there was a

latent hyperthyroidism either as the sole cause of the trouble or present as an additional burden on the heart already affected with some other organic lesion. One unusual case is included in this group in which there were associated attacks of synocope due to heart-block. Following subtotal thyroidectomy the attacks disappeared, and the patient has been much improved following the operation.

Dedication to Professor Wenchebach. Wien. Arch. f. inn. Med. **18**: 1, 1929.

Professor Wenchebach's tenure of office as professor of medicine being terminated, he has been celebrated by a special issue of his paper, "Wiener Archiv für innere Medizin." V. Falta has edited and dedicated the volume which contains contributions from twenty-four of Wenchebach's students. The greater part of the volume contains cardiological papers. A long paper by Falta on renal diabetes and diabetes mellitus forms a notable exception.

Hans Kutschera Aichbergen (page 209) has written on cardiac asthma. He finds that in many cases of vascular failure the defect lies in the cardiovascular system itself rather than in extraneous factors such as anemia or too great demands by the organism. Among cardiovascular causes cardiac weakness in itself forms an important factor, and this has been made the subject of investigation.

In the early stages cardiac weakness can well be treated by rest and digitalis, later it becomes increasingly refractory to treatment until at last permanent failure sets in.

To explain the pathology he finds it useless to consider permanent cardiac damage, but it is necessary to look for such changes as are reversible when treated with rest and digitalis. In many cases the conditions which lead to cardiac decompensation correspond closely to the process of fatigue which occurs in any muscle.

Therefore, in cardiac weakness we are dealing with nonspecific fatigue phenomena, characterized by chemical and physicochemical changes, most important among which are changes in the concentration of the substances furnishing energy and increase in the permeability of the muscle cell membranes; that is, changes in the colloid phases. In cardiac as in other muscles the main changes occur in the phosphatides, which are decreased everywhere in the decompensated heart. Digitalis therapy was found to increase the phosphatides.

In cardiovascular insufficiency of infections not only the heart but muscle of the entire cardiovascular system is weakened. In these cases the heart muscle is found to suffer in a manner similar to that of chronic heart failure. This increased fatigability in infections is explained by suprarenal damage, for in the suprarenals as in the heart muscle, the damage is manifested by decrease in phosphatides. This is particularly interesting because it is related to muscle fatigue generally. This finally leads the author to a hypothesis of cardiovascular asthenia in infectious diseases as having their origin in suprarenal insufficiency.

Erich Zdansky (page 461) contributes a paper on pulmonary stasis in cardiac disease. The study is on the basis of roentgenological, clinical and anatomical investigations. In chronic congestion the lymph vessels of the interstitial tissues are dilated and the mediastinal lymph glands enlarged; this is mostly due merely to transudate, though infection seems to play a part in the enlargement of the hilus glands.

The edema is not evenly distributed throughout the lung but prefers the connective tissues around vessels and bronchi, especially in their bifurcations and their central parts. Probably this is due to diminished respiratory movements, and this makes absorption more difficult.

These factors, increase of lymphatic structures and uneven distribution of fluid in the lungs explain together the roentgen picture. The vascular pattern becomes

widened and increased, the hilus shadows become enlarged and indistinct, and indistinct "floceuli" are formed in the pulmonary fields.

In the x-ray picture may also be seen circumscript accumulations of transudate inside the lung; these are without relation to vessels and bronchi. They may be localized in areas and may occupy a lobe or an entire lung field. The pathogenesis of some of these is known as hypostatic pneumonia in dependent parts of the lungs.

But there are other, so far unknown, causes of these circumscribed areas of edema; indurations of lung tissue, caused by decreased respiration or anatomical narrowing of efferent lymph vessels. Tuberculous or anthrocotic changes in hilus glands may obstruct the drainage of transudate. Pleural adhesions may decrease respiratory movements with stasis resulting.

The clinical results of this uneven drainage will be a tendency to asymmetrical bronchitis, areas of consolidation and predisposition to pulmonary edema. In the roentgen pictures these lesions may often appear as focal pulmonary infiltrations, miliary disseminations, extensive pneumonic processes, infarcts, etc. A differential diagnosis from these lesions may be difficult. The swelling of the hilus glands may become so extensive as to become visible on the roentgen pictures, where they appear with indistinct margins owing to the general moisture of the lungs. Pleural adhesions may often be diagnosed by edematous infiltrations.

The problem of coronary thrombosis is attracting attention also on the continent. Richard Singer, p. 421, in this volume describes its "Clinic and Therapy" on the basis of 20 cases. The symptoms are: pain of the angina pectoris type, not relieved by nitroglycerin, and fever. If the left ventricle is affected, left ventricular insufficiency is indicated by Cheyne-Stokes breathing. Electrocardiographic disturbances occur in almost all cases; during the first forty-eight hours, the findings are typical, after this many variations may occur. Most commonly there is an isoelectric, diphasic or negative T-wave, widening or splitting of the R-wave; frequently the Q-wave is remarkably deep. Tachycardia, bradycardia and extrasystoles were seen as well as evidence of decompensation and digestive symptoms.

The prognosis depends on the amount of cardiac damage and danger of recurrence. Seven of the patients died. The treatment consists in absolute rest in bed, morphine and quinidine. About two weeks after the attack the author gives a course of euphyllin intravenously. Digitalis is only given in small doses in cases of decompensation. If angina and hyperesthesia persist after the acute stage, the author prescribes Zülger's heart hormone and roentgen therapy.

Wassermann (page 449) contributes a small paper on the origin of heart failure psychoses. If these occur during the course of decompensation, they are to be ascribed to left ventricular insufficiency, part of which forms the cerebral anemia with Cheyne-Stokes breathing. Therefore in case of psychical symptoms in the course of heart failure the breathing should be closely watched. Separately from these he considers the psychoses which accompany the end of decompensation (terminal or agonal psychoses); these have a very bad prognosis.

The psychoses may precede the clinical decompensations in the form of slight nocturnal delirium, and they may last until the end. They belong to the category of "fear" psychoses and are of central origin, probably due to insufficient circulation resulting in lack of oxygen. This is explained by both their nocturnal exacerbation (sleep anoxemia) and their prevalence in cases of aortic insufficiency. The prognosis is intimately connected with that of the cardiac condition; where Cheyne-Stokes breathing occurs, oxygen therapy is of great value.

Alfred Weit (page 457) reports two cases of cardiac lesions without disturbance of function; one of a man with a bullet in his heart. The lesion presumably dates from the war, but he had no idea of its presence; not even at the time of the injury did he have symptoms; his attention at the time was drawn to a gunshot wound of the arm. The author refers to another case where a man shot himself;

the bullet severed His-Towara's bundle and produced complete heart-block; after this it became lodged in the posterior mediastinum. It produced no other effects.

The author then reports a case of peculiar right-sided enlargement of the heart, possibly an aneurysm. The remarkable thing is that a very marked enlargement has persisted for over four years without producing symptoms.

Also Hans Dietlen (page 19) contributes a case report of peculiar cardiac enlargement where the diagnosis of mitral stenosis and tricuspid insufficiency seems far from certain; neither his nor Weil's cases are accompanied by autopsy reports, all the patients still being alive.

H. Elias and J. Goldstein (page 29) differentiate between congestive heart failure of mitral stenosis and that of mitral insufficiency; they find edema in mitral stenosis is a rare and late manifestation. When it does occur, it is much less extensive than edema of mitral insufficiency. This difference holds good for all ages. On the other hand hepatic enlargement is more frequent in mitral stenosis than in insufficiency. The same holds true regarding evidence of cerebral anemia.

Fischer and Schur (page 151) record respiratory changes in the height of the pulse; they register the pulse sphygmographically over an artery compressed proximally with a cup. During inspiration the pulse becomes smaller, during expiration larger, during the interval it retains a medium size. In adherent pericarditis it became smaller during inspiration; it was largest during the respiratory pause. The respiratory changes in size are more marked than the respiratory changes in rhythm. They explain the changes in size as being due to changes in intrathoracic pressure. Finally they propose to change the term pulsus paradoxus to "Wenchebach's pulse."

Rudolf Strisower (page 445) reports on a series of experiments on feeding to rabbits cholesterol and other substances considered in the pathogenesis of hypertension. The experiments were entirely negative.

Verhandlungen der Deutschen Gesellschaft für Kreislaufforschung. Second Meeting at Bad Neuheim, March 4 and 5, 1929.

H. Siegmund: Concerning Nonsyphilitic Aortitis.

The author calls attention to lesions of the aorta; these accompany infections, particularly ulcerative and polypous endocarditis. They may, however, occur without accompanying valve defects.

They are characterized by mesaortitis without pus formation, destruction of elastic fibers and extensive destruction and scarring of the intima. In some cases Streptococcus viridans may be found in the blood stream. Some of these cases macroscopically look very much like luetic mesaortitis.

The lesions originate by direct implantation of more frequently by emboli through vasa vasorum. The resulting necrosis and fibrosis may be accompanied by atherosclerosis. The author also found healed lesions in routine autopsies.

Besides in ulcerative endocarditis similar lesions were found in cases of scarlet fever and rheumatic fever.

H. Mussler: Die Gesetze des Blutdruchablaufes.

The pulse pressure is a measure of the energy given to the blood stream by the heart. When the blood pressure increases, through drugs or through exercise, the diastolic pressure decreases. This is only possible with increased blood velocity which means improved circulation. At a certain increase of pulse pressure the diastolic pressure becomes constant. This is called the critical amplitude. If the pulse pressure is still further increased, the diastolic pressure increases. This results in a rapid increase in systolic pressure, this depreciates the general circulation, as the heart has a greater "resting pressure" to overcome. This results in uneconomical working. The play between normal and critical amplitude is a measure of vascular

elasticity and of cardiac reserve; it is also dependent on obstructions to the circulation. While the normal pressure is 50 mm. Hg, the critical lies about 70 to 80. In the clinical observation of the patient, the pulse pressure readings are of great importance.

P. Iversen: Oedem-pathogenese mit Bernehrungen Über Azitiepathogenese bei Herzinsuffieienz.

It is in the capillaries that the shifting of water occurs from the vascular system to the intercellular connective tissue spaces. In order to understand the nature of edema one must realize that in the capillaries there are two kinds of pressure, a hydrostatic and an osmotic which is 2-300 times greater than the former. But only the fraction due to the colloids is effective, as the capillary wall is permeable to the dustalloids, which there can exert no osmotic pressure. These two pressures act against each other, and it is upon changes in the equilibrium between them that edema depends. That is, edema occurs when the hydrostatic pressure exceeds the osmotic. This may occur through increase of hydrostatic and decrease of osmotic pressure, or through a combination of the two.

The colloid osmotic pressure depends upon the percentage of protein and on the molecular size thereof. If the molecular size is greater, the osmotic pressure is smaller. Globulin has a larger molecule than albumin.

In nephrosis both the total percentage of protein and the albumin fraction in the serum are decreased. Both tend to decrease the colloid osmotic pressure below the normal hydrostatic pressure.

In heart failure patients the stasis is the important factor, because here the hydrostatic pressure increases above the colloid osmotic pressure, which furthermore is somewhat decreased partly by hydremia and partly by decrease of serum albumin through albuminuria. Besides some small but osmotically very active molecules are exceeded into the urine, this is especially marked in long-persisting but slight albuminurias.

In order to overcome edema, it is necessary to reestablish the normal equilibrium. In heart failure the cardiac tonics are used to improve the peripheral circulation; thereby the venous system is relieved, and the hydrostatic pressure in the capillaries falls, the urine secretion increases and the albuminuria disappears and the hydremia is overcome.

In ascites the same rules hold true; the varying amounts of albumin found in the exudate depend upon the stage of resorption, the greater absorption, the higher the percentage of albumin in the remaining fluid. Complete absorption only occurs after splitting up of the protein molecules.